THE VALUE OF CLINICAL TRIALS: A NEW ZEALAND CASE STUDY

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STATEMENTS AND DECLARATIONS

DECLARATION OF ORIGINALITY

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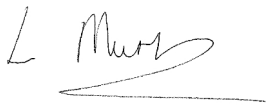
STATEMENT OF ETHICAL CONDUCT

The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University. This study has received ethical approval from the Tasmanian Social Science Human Research Ethics Committee reference number H10522, the New Zealand Northern Y Regional Ethics Committee reference number NTY/09/04/037 and the Manukau Institute of Technology Ethics Committee reference number E09/EXP/19 (nty/09/04/037).



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ABSTRACT

Objective:

The research question addressed in this thesis is - 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?'

Methods:

The research design is a simultaneous parallel mixed method design that incorporates two strands (1) A quantitative analysis of economic outcomes and (2) a qualitative analysis of perceived value. In the first strand, quantitative methods draw on the data relating to two sponsored clinical trials. The data include Ministry of Health data, The Centre for Clinical Research and Effective Practice (CCRep) profit and loss statements, Counties Manukau District Health Board (CMDHB) annual reports and Chronic Care Management (CCM) data and results from a health outcome co-study. The second strand uses qualitative methods to explore the benefits and costs of sponsored clinical trials perceived by stakeholders. The study gathers data using focus groups, interviews and surveys and adopts a qualitative descriptive approach followed by a phenomenographical analysis.

Results: The economics outcomes strand finds that CCRep, CMDHB and New Zealand society all derive financial benefits from these trials. The magnitude of the economic benefits differs depending on the perspective taken. Both CCRep and CMDHB have benefits that are positive but small. The largest and potentially the most controversial benefit is a benefit to New Zealand society of over 373,000 dollars. The qualitative results suggest that the benefits of conducting sponsored clinical trials within a publicly funded New Zealand hospital outweigh the costs in respect of all stakeholder groups. The results allow classification of the stakeholders into three layers: societal; where benefits and costs are filtered by political and social opinions; organisational; where benefits and costs are seen in terms of their influence on organisational functions and personal; where benefits and costs are seen as contributing to the psycho-social, cognitive, physical and behavioural needs of individuals.

Conclusion: Public bodies must be mindful of the wider economic, social and cultural implications of their activities. This study demonstrates the value created from conducting clinical trials. The adoption of qualitative and quantitative methods to measure this value produces a more rounded analysis than would be the product of either approach on its own.

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Finally, and above all others, I am deeply grateful to the patience and loving support of my husband, Patrick and children Samuel, Hannah and Leah and for their ability to provide balance and where necessary healthy distraction throughout the journey of my thesis.

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LIST OF ABBREVIATIONS

ACC	Accident Compensation Commission
ACE	Angiotensin-converting enzyme
AIDS	Acquired immune deficiency syndrome
ACP	Average cost per participant
BCA	Benefit cost analysis
CCA	Cost consequence analysis
CCRep	Centre for Clinical Research and Effective Practice
CEA	Cost effectiveness analysis
CEO	Chief executive officer
CCM	Chronic Care Management Programme
CTTI	Clinical Trials Transformation Initiative
CMA	Cost minimisation analysis
CMDHB	Counties Manukau District Health Board
CRO	Clinical research organisations
CUA	Cost utility analysis
DHB	District Health Board
FDA	The Food and Drug Administration
GTPS	General Transaction Processing System
GST	Goods and services tax
HR-QOL	Health-related quality of life
HIV	Human immunodeficiency virus
IFA	The International Federation of Accountants
IRB	Institutional Review Board
ISPOR	The International Society of Pharmacoeconomics and Outcomes Research
Labs	Laboratory Claims Data Warehouse
Medsafe	The New Zealand Medicines and Medical Devices Safety Authority
MOH	Ministry of Health
NGO	Non-government organisation
NPV	Net present value
NZACRes	New Zealand Association of Clinical Research
NICE	National Institute for Clinical Excellence
OECD	Organization for Economic Co-operation and Development
PHARMAC	The Pharmaceutical Management Agency
PrS	Probaility Sampling
PuS	Purposive Sampling
QALY	Quality adjusted life years
QOL	Quality of life
RMI	Researched Medicines Industry Association (now Medicines New Zealand)
SLY	Statistical life year
TTO	Time-trade-off
VAS	Visual analogue scale
VSL	Value of a statistical life

1. INTRODUCTION TO THE STUDY

The research question in this study is: 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?' Accountants have an important role to measure the value of government services, programs, and assets; develop reporting systems that track value changes, and regularly communicate their effectiveness in value creation. The concept of value and the accounting discipline are intricately related. This thesis, however, challenges the conventional view of 'value' that underpins many traditional views of accounting.

To illustrate the concept of value, this thesis reports the results of an empirical study that examines the value created by conducting sponsored clinical trials in a publicly funded New Zealand hospital. The focus of this study is primarily upon two long-term clinical trials performed within a clinical research unit over eight years (2001 – 2009). This eight-year period includes recruitment, trial and follow-up stages.

This chapter proceeds as follows. The first section considers the nature of value and challenges some of the conventional accounting notions of value. The chapter identifies the importance of value and establishes the context of the case study by explaining the nature and function of clinical trials and their role within the New Zealand health system. The chapter then justifies the thesis highlighting the importance of the study outcomes to public and social policy and the studies academic significance. The chapter identifies the stakeholders and then presents an overview of the research method including the research design, sampling techniques and data collection and analysis. The chapter next establishes the combined potential of qualitative and quantitative methods to produce a strong evaluation of clinical trials. The conclusion of the chapter provides an outline for the rest of the thesis.

THE NATURE OF VALUE

Nørreklit, Nørreklit and Mitchell (2010 p733) describe accounting as,

> *a task that requires the identification and selection of the real world events upon which the information is to be based, the measurement of these events and the assimilation of these measurements into an appropriate form for presentation to and employment by the information user*.

Within '*all theories of accounting lies a theory of value and the origin of profit'* (Bryer 1994 p313). The creation of value is the key motivational force in market economies (Wheeler, Colbert and Freeman 2003). Accounting value in the conventional view is limited to actions involving economic information and is characterised by denomination in money amounts (Boyce 2000). The accounting approach to value is the easiest form of value to explain because accounting concepts have fewer emotions attached than many other measurements of value (Hull 1944). However, a restricted view of accounting involving only economic information places significant artificial constraints on the possibilities of what might be accounted for when considering accountability in a broad sense (Gray, Owen and Adams 1996). Out of this concern, alternative accountings focussing on social factors have developed (Boyce 2000). Social accounting involves the valuation of social costs and benefits that are quantifiable in money terms, and the valuation of and accounting for social impacts that are not easily and meaningfully quantifiable in money terms (Boyce 2000). As Gray (2006 p809) observes,

> *....there is other 'value' than that of money – the value of life, the value of society, the value of quality and, if one is of a religious bent, the value of creation itself*.

Value, therefore, may refer to concepts of quantity, amount, or entity or concepts of worth, and different actors perceive it in different ways (Wheeler et al. 2003).

VALUE AND HEALTH

New Zealand's health system, like those of many other countries, faces significant challenges, for example, pressures from an ageing and growing population, new technology and medicines, unsustainable funding and shortages of health professionals (McClellan, McGinnis, Nabel and Olsen 2008). Healthcare needs to adapt to meet these challenges (McClellan et al. 2008). Porter (2010) argues that central to managing health care in challenging economic times is the improved ability to define and measure value in health care. A rigorous approach to defining and describing outcomes is important (Porter 2010 p2477):

> *Since value depends on results not inputs, value in health care is measured by the outcomes received, not the volume of services delivered, and shifting focus from volume to value is a central challenge. Nor is value measured by the process of care used;*

> *process measurement and improvement are important tactics but are no substitutes for measuring outcomes and costs.*

The 'outcome' used in the assessment of value in favourable outcomes minus adverse outcomes or put another way value equals effectiveness minus harm (Gray 2007). Therefore, more resources do not always produce an increase in value because the balance of good to harm changes as the amount of care increases (Gray 2007). In addition, Porter (2008 p162) identifies the existence of multiple outcomes for any one condition:

> *Health outcomes refer to the set of objective outcomes, not just patient perceptions of outcomes which can be biased toward the service experience. There is not just one outcome of care for any health condition, but multiple outcomes that jointly constitute value. Patient circumstances and preferences will affect the weighting of these outcomes to some degree…*

Porter suggests that all stakeholders can contribute towards improvement in healthcare delivery by organising their activities around value as a central goal in health care Porter (2008 p172).

Value must be the fundamental goal of any healthcare system. Measuring value, and improving it, must become the driving force for every participant in the system.

THE EMPIRICAL STUDY

This thesis reports on a case study that combines accounting and economic methodologies to measure the value created and captured by two clinical trials. This study applies a BCA to assess the value of conducting clinical trials in a publicly funded New Zealand hospital. BCA is one way to measure value and value creation. The academic literature identifies close links between value and BCA (see for example, Sen 2000, Lenman 2000, Hanley and Splash 1993 and Baum 2010).

The current study considers the benefits and costs from several different perspectives. The study first quantifies the benefits and costs from the perspective of:

1. the Centre for Clinical Research and Effective Practice (CCRep);
2. Counties Manukau District Health Board (CMDHB);
3. New Zealand society.

It next establishes the benefits and costs of sponsored clinical trials as perceived by:

1. trial participants;
2. trial participants' family member and caregivers;
3. Counties Manukau District Health Board staff;
4. researchers;
5. the Counties Manukau community;
6. government, government bodies and politicians; and
7. members of the pharmaceutical industry.

The research builds on a health outcomes study that involves a retrospective cohort study of changes in a clinical trial participants' health status and mortality rates. Although a team of medical researchers conducted that study (i.e. the current author was not involved), it contributes to the current research as it reports patients health outcomes and forms the platform for the evaluation of clinical trial costs and perceived outcomes.

The current study identifies a single case study site (CCRep) to conduct the research as this provides more opportunities for in-depth analysis (Saunders, Lewis, and Thornhill 2007). Yin (2003 p13) defines a case study as '*an empirical inquiry that investigates a contemporary phenomenon within its real-life context'*. It is a good method for examining 'what' questions which enquire about events over which the investigator has little or no control (Saunders, Lewis, and Thornhill 2007).

The current study adopts a pragmatic world view that focusses on '*actions, situations, and consequences*' (Creswell 2008 p10). A pragmatic worldview has a concern with applications that work (Patton, 1990) and, therefore, allows researchers to use methods that are appropriate to the research problem (Creswell 2003). A pragmatic world view provides a sound philosophical underpinning for mixed methods studies (Tashakkori and Teddlie 1998, Morgan 2007) and is, therefore, appropriate for the current study.

The current study comprises two long-term clinical trials performed at CCRep over eight years (including pre-trial, trial and follow-up periods) to identify the benefits and costs of clinical trials. The two studies provide a representative sample of clinical trials and provide sufficient participants to ensure a good representation of benefits and costs while remaining manageable in terms of matching sufficient case controls. It adopts a simultaneous parallel mixed methods design (Teddlie and Tashakkori 2009) in which it collects different but complementary data on the outcomes of sponsored clinical trials. A strand of a research design is a phase in which a

qualitative or a quantitative approach is used in the method of study, in data collection procedures, or in data analysis (Tashakkori and Teddlie 2003, Teddlie and Tashakkori 2009). Simultaneous parallel mixed method design is a research design in which there are two relatively independent strands: one with qualitative data collection and analysis techniques and the other with quantitative data collection and analysis techniques (Teddlie and Tashakkori 2009). The strands run concurrently. The design builds on a retrospective cohort study of the health outcomes from clinical trials. Although a team of medical researchers conducted that study (i.e. this author was not involved) it forms one of the three strands of the research owing to its providing the platform for the other two strands, namely the multiple stakeholder perception strand and the economic outcomes strand.

The 'reality' of a case study can be considered in terms of 'worlds' 'realms' or 'orders' which enable accounting research to provide opportunities for researchers to explore multiple realities (Llewellyn 2007). Llewellyn (2007) identifies five different realities: (1) the physical; (2) structural; (3) agential; (4) cultural and (5) mental worlds. The physical world comprises the material, physical, organic or natural realms. The structural world includes roles, distributions, institutions and systems. The agential world is the world of transformation that is made up of human projects and of people trying to make things happen. The cultural world includes knowledge, concepts, values, beliefs, ideologies, signification and symbolism. Finally, the mental world is the realm of perception, thought, feelings, desires, emotions and predispositions. The empirical study described here identifies value created in each of these realities.

The nature of the study, the way in which it develops and the evolution of the research team all play a part in shaping the current study. The genesis of the current study lies in a health outcomes study by the medical research team at the Centre for Clinical Research and Effective Practice (CCRep). Relative to research units that conduct clinical trials in Australasia, CCRep has conducted a significant number of clinical trials (Counties Manukau District Health Board, 2009a) and CCRep clinicians believe that they have developed the expertise to add value through these trials.

The health outcomes study uses quantitative methods to evaluate health outcomes from two randomised clinical trials with a cohort control group. While the study would serve to raise CCRep's profile in this area, the medical team felt that it should be extended to an economic evaluation. Consistent with Babour and Barbour's (2003) recommendation of collaborative

exercises and parallel data collection as an efficient and effective research process when resources are scarce, they sought a research partner to evaluate the economic outcomes for the two clinical trials and cohort control groups. This is CCRep approached the School of Nursing at a local institute of technology for assistance in recruiting a team and researchers from the School of Business expressed interest.

During a brainstorming session by researchers from the Nursing (qualitative focus) and Business Schools (mainly quantitative focus), they concluded that a quantitative evaluation alone would not tell the whole story, because only a qualitative study would reveal a sense of the value that stakeholders place on clinical trials. They also recognized the difference in the relative sensitivity of data collected from quantitative and qualitative studies. Consistent with Moffatt, White and Mackintosh (2006), a qualitative study may identify significant impacts on stakeholders, whereas a large health board may not find practical or economic interest in a quantitative study indicating that the economic outcome of the trial is not significantly positive in economic terms.

During the early preparations for the project, the CCRep research team suggested that it would be advantageous to include a PhD student in the team. A member of the team subsequently committed to a PhD, and two other members acted as the principal and co-supervisors. The researchers at CCRep managed the health outcomes project and maintained a deep interest in all other aspects.

MICRO, MESO AND MACRO LEVEL ANALYSIS

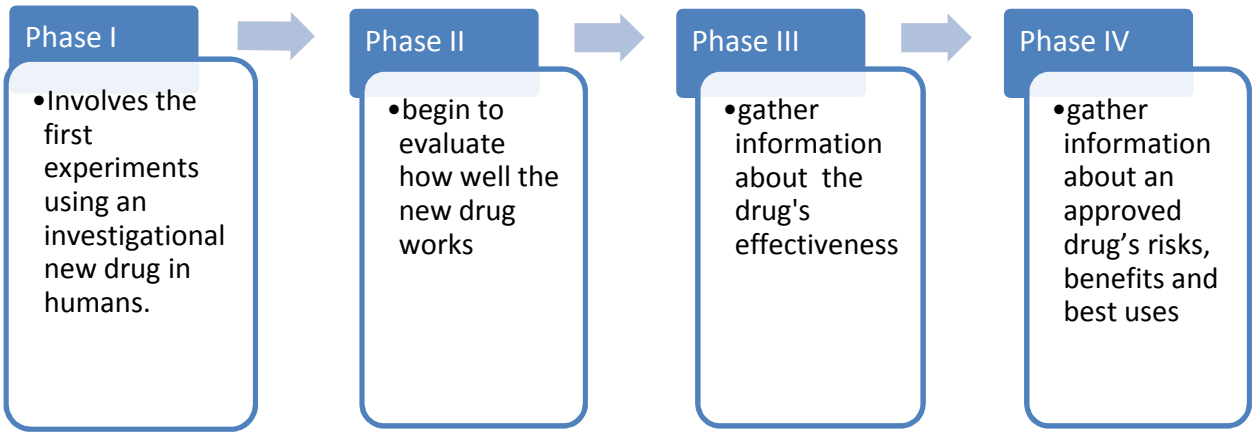
In addition to the above approach to classifying stakeholders, the current study group's stakeholders at a micro–meso–macro analytical framework (Dopfer, Foster and Potts 2004). Micro-level studies describe buying and selling and supply and demand (Forge 2009). Qualitative data are especially good at exploring the micro-level and revealing feelings and emotional responses that are not discovered through quantitative research. Quantitative data are best for investigating the economic benefits and costs of clinical trials. The current study investigates micro-level benefits and costs from the perspective of the research unit (CCRep). Macro-level analysis is concerned with aggregate totals and the large-scale effects of micro-level activity (Forge 2009). The current study analyses macro-level benefits and costs of sponsored clinical trials from the perspective of society as a whole. Meso-level analysis occurs

between the micro and macro-level and considers *'the context, inter-dependence and structures in which micro and macro-economic forces operate'* (Forge 2009 p43). The current study analyses meso-level benefits and costs from the perspective of the CMDHB.

STUDY CONTEXT

Clinical trials are the most reliable way to assess the efficacy and safety of health interventions (Jull, Wills, Scoggins, and Rodgers 2005). They provide information for national treatment guidelines on patient management and are required for approval and registration of new medicines. The evaluation of new pharmaceutical products through clinical trials plays an important role in modern evidence-based medical practice.

FIGURE 1-1 PHASES OF CLINICAL TRIALS



Clinical trials follow laboratory testing in cell and animal studies and occur in four distinct phases, all of which involve humans. Figure 1.1 illustrates the phases of clinical trials. Phase I trials are the first experiments using a new drug in humans and normally involve healthy participants. Researchers design these studies to determine how the drug interacts with the human body. They examine the effectiveness of and any side effects associated with the new drug. Information from Phase I studies is used to design Phase II trials. Phase II trials evaluate how well the new drug works and continue to test the safety of the new drug in a larger group of patient volunteers. Phase III studies assess the effectiveness of a new drug as compared with current standard treatments. Researchers select participants randomly for either a drug trial group or a placebo control group. As these trials involve large numbers of participants and normally occur over several years, the costs are higher than earlier trials in this sequence. I examine Phase

III studies in this research. Phase IV trials are undertaken after a new drug has been approved for use on humans. Researchers continue to gather information about the drug's long-term risks or benefits and possible new uses. Data Researchers may also gather data on how the new drug interacts with other medications (Medicines New Zealand nd).

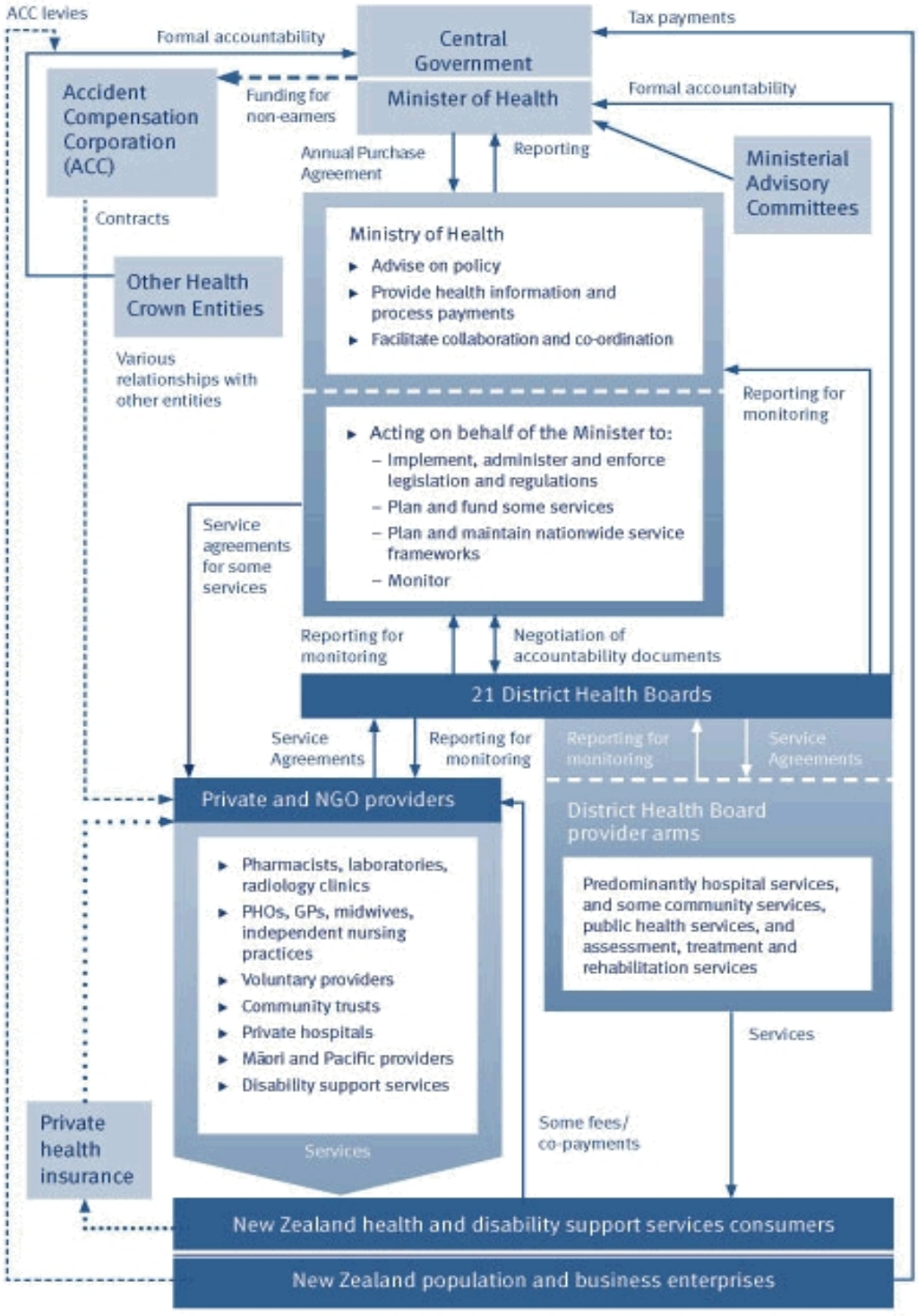
An effective drug can bring relief to a great number of people. Clinical trials around the world feed information into the international knowledge base although societal values may influence the benefits of clinical research among countries (Buxton, Hanney and Jones 2004). This variation justifies local research. Zycher, DiMasi, and Milne (2008) highlight the interdependence of public and private sector contributions to the discovery of new drugs. They suggest that public and private sector research complement each other and are equally necessary for new drug development although the balance between public and private contributions varies from country to country.

In New Zealand, clinical research settings range from fully government-funded research centres such as those within universities and some hospitals, to commercially operated research centres, as is the location of the study for this research. CCRep facilitates sponsored clinical research for CMDHB. CMDHB has shown leadership in establishing CCRep as a vehicle for conducting clinical research. A benefit cost analysis[1] (BCA) will allow an evaluation of this decision and provide guidance for other health boards who may be considering developing a similar research structure. CCRep's community focus combined with the accessibility of their Middlemore Hospital site makes this an ideal location for this study.

New Zealand has an integrated public health system with twenty health boards and eighty-five public hospitals. Publicly funded health care accounts for eighty percent of all health spending. Private spending such as patient co-payments for general practitioner visits, prescriptions or insurance, accounts for the remainder (New Zealand Treasury 2009). The government expenditure is higher than Australia where, government funding covers sixty seven point five percent of health care expenditures with private sources covering the remaining (World Health

[1] Benefit-cost analysis (BCA) is also referred to as cost–benefit analysis (CBA) by some authors. BCA places the emphasis first on benefits followed by costs. The terms are otherwise equivalent.

FIGURE 1-2 STRUCTURE OF THE NEW ZEALAND HEALTH AND DISABILITY SYSTEM. (SOURCE: MINISTRY OF HEALTH nd).



Organisation 2008). The district health boards (DHB) have a degree of autonomy in how they choose to achieve the health care objectives for their region. Figure 1.2 illustrates the New Zealand health care system. The focus of this research lies with the provider arm, which provides mainly hospital-based services. It also affects the private and non-government organisations that provide pharmaceuticals, laboratory testing and outpatient primary care.

The DHB has formal accountability to the Central Government through the Minister of Health and receives government funding to provide district health services. Public hospitals provide hospital treatment free of charge, which makes the New Zealand health system different from that in many other countries that conduct clinical trials. In New Zealand, pharmaceutical companies have to rely on publicly funded hospitals to gain access to participants and to have a locality that is equipped to do clinical trials. Where an independent hospital is involved in the trials, the research is separated from the sponsoring company and is, therefore, less likely to be seen to be to be biased.

The New Zealand environment has other features that distinguish it from other countries in which clinical trials are undertaken. One of the most important of these is the recognition that New Zealand Maori as the indigenous people of New Zealand have a unique set of rights negotiated under the Treaty of Waitangi, a document signed in 1840 between the British Crown and Maori leaders. Recent interpretations of the Treaty establish a requirement that Maori have the opportunity for partnership and participation in the systems and structures of society and that Maori values and beliefs are protected (Hudson 2004). The Health Research Council of New Zealand reinforces the importance of treaty obligations to the research environment (2002 p1):

> *The principles of partnership and sharing implicit in the Treaty should be respected by all researchers and, where applicable, should be incorporated into all health research proposals.*

As is common in other Organisation for Economic Co-operation and Development (OECD) countries, New Zealand has processes in place to control the research, marketing and promotional activities of the pharmaceutical industry. Processes include: (1) Standards and Codes for good clinical practice (GCP) in research; (2) New Zealand Research Ethics Committees; (3) New Zealand Medicines and Medical Devices Safety Committee (Medsafe); (4) The Pharmaceutical Management Agency (PHARMAC) (5) New Zealand Legislation.

TABLE 1-1 PRINCIPLES OF ETHICAL REVIEW (SOURCE: MINISTRY OF HEALTH 2006 P6).

Main principles	**Additional concerns for Maori**
Respect for persons	Respect for Maori collectives whanau, hapu and iwi
Informed consent	Gaining consent of collectives
Privacy and confidentiality	Collective ownership of information
Validity of research proposal	Kaupapa Maori and Maori-focused methodologies
Minimisation of harm	Minimising harm to te taha whanau (family and community), te taha hinengaro (emotional wellbeing and state of mind), te taha wairua (spirit), te taha tinana (the body or physical self)
Justice	
Cultural and social responsibility	Cultural diversity, koha (donation, present or gift)
Compensation for research participants	

A robust New Zealand system of ethical review has an important role in maintaining ethical standards in clinical research conducted within New Zealand. Seven health and disability ethics committees carry out ethical review of clinical trial. Six of these committees consider applications for research within their region. The Multi-region ethics committee considers applications across multiple regions. Principles set out and explained in detail in the operational standards issued by the Ministry of Health govern ethical review in New Zealand (Ministry of Health 2006). The operational standards also provide Maori interpretations of ethical principles as a way of safeguarding specific Maori culture and values. Table 1.1 shows how the operational standard incorporates Maori concerns. This is an important aspect to consider in obtaining ethics approval to conduct clinical trials in New Zealand. These principles mean ethics approval documents developed overseas must be adapted to meet these additional standards. The pharmaceutical industry works to agreed standards that involve practices and behaviours informed by international codes such as the Nuremburg Code (nd), the declaration of Helsinki (World Medical Association nd) and the Belmont Report (International Review Board nd).

Edwards, Lilford and Hewison (1998) undertake a review of 61 studies of the perspectives of patients, the general public and healthcare professionals on the ethics of clinical trials. Of these, 53 use quantitative and seven use qualitative methods alone, while one study uses both. They identify stakeholder concern surrounding the ethics of clinical trials, are highly critical of the

quality of the research methods used and call for further research into '*what well informed members of the public really think about trials'* (p1211).

Foëx (2008 p98) summarises the often complex ethical issues associated with trial conduct:

> *For all the regulation of clinical trials, there remain areas of controversy. Is it reasonable to compare a new treatment with placebo? That will depend on whether placebo is the current standard of care. Is it ethical to stop a trial early for commercial reasons? Does commercial funding of trials influence their results? There is certainly evidence to suggest publication bias. The issue of informed consent remains problematic for trials involving children, incompetent adults, emergency situations and the critically ill. However, all these groups have the right to benefit from medical advances, which can be made only through clinical trials.*

Medsafe has systems of pre-marketing approval for all new medicines and post-marketing surveillance of medicines and medical devices in use in New Zealand. This includes monitoring adverse reactions to medicines used in New Zealand; testing marketed medicines against product quality standards; handling complaints and investigations, and auditing and licensing medicine manufacturers and pharmacies. PHARMAC has control over the expenditure on and usage of prescription medicines. Considerable legislation governs the conduct of the pharmaceuticals industry within New Zealand. Key legislation includes Medicines Act 1981, Medicines Regulations 1984, Commerce Act 1986, New Zealand Bill of Rights Act 1990, The Privacy Act 1993, The Accident Rehabilitation, and Compensation Insurance Act 1992.

MOTIVATION FOR THE RESEARCH

The motivation for this research lies with the significance of the study outcomes to public and social policy and the contribution to the development of theory and method.

CONTRIBUTION TO PUBLIC AND SOCIAL POLICY

Currently there is no readily available information on the conduct of clinical trials in New Zealand. In particular there is no agreement on the number of trials, cost of trials, percentage of trials by phase, percentage of trials by therapeutic area or the sources of funding for trials in New Zealand (commercial or academic, local or international). Further, recent literature reveals little

information on the benefits and costs related to clinical trials in New Zealand, whether they relate to health outcomes, stakeholder perceptions or economic outcomes. Watson (2006) authored one of the few New Zealand studies and the first of its kind based on New Zealand data, albeit commissioned by Pfizer Pharmaceuticals (i.e. not an independent study) and based on secondary data. He considers that sponsored clinical trials could have an important role in New Zealand's health system by providing the potential to contribute to reducing the costs of New Zealand DHBs, retaining and developing a pool of internationally recognised New Zealand researchers and sustaining New Zealand's clinical research infrastructure. At the same time, they allow New Zealanders timely access to new drugs. International studies have produced a variety of results on the benefits and costs of clinical trials. (See, for example, LaFleur, Tyler and Sharma 2004, McDonagh, Miller and Naden 2000 and Braunholtz, Edwards and Lilford 2001) whose studies are reviewed in the next chapter. These studies suggest that clinical trials offer potential benefits to trial participants and potential cost savings to the New Zealand health sector. The current study will examine the realities of these potential benefits.

The first recorded New Zealand clinical trial was published in the New Zealand Medical Journal in 1955 (Neal, Rodgers, Mackie, and MacMahon 1996). This marked the beginning of a growth phase in clinical research in New Zealand according to Jull et al. (2005) who review trials conducted between 1998 and 2003. They investigate the number and type of clinical trials in New Zealand (Jull et al. 2005). Their findings show that the majority of ethics applications came from the Auckland and Canterbury regions and that most of these applications were for Phase III trials involving pharmacological agents. Fifty percent of trials were in the fields of cancer, cardiovascular disease, and respiratory disease. Ethics approval was sought for 665 clinical trials over this six year period and the number of trials conducted each year was relatively consistent (1998, 118 trials; 1999, 91 trials; 2000, 103 trials; 2001, 104 trials; 2002, 108 trials; 2003, 141 trials).

Commercial pharmaceutical companies sponsor most clinical trials in New Zealand public hospitals. The development of new pharmaceutical products involves considerable resources. Murphy and Topel (1998) assert that the pharmaceuticals industry, when compared to other industry's, is the highest investor in research and development as a percent of net sales and that the pharmaceutical industry invests 10.4 percent of net sales into research activity. Clinical trials

are the final stage of this development activity. The current study will provide a better understanding of the benefits and costs of clinical trials within New Zealand.

Currently clinical trials in New Zealand are estimated to be worth between $12 million to $30 million per year (New Zealand Parliament 2010). Internationally, recent growth of sponsored clinical trials has created fears that sponsorship arrangements may lead to too much interference in the research process. Angell (2008) asserts that since the 1900s pharmaceutical companies have insisted on control of their clinical trials to the point that now '*in some multicentre trials, authors may not even have access to all of their own data*' (p1069). She is concerned that competition for clinical trial contracts has applied pressure on research centres '*to accept Drug Company terms that would once have been unthinkable'* (p1070).

TABLE 1-2 PROJECTED NUMBER OF PARTICIPANTS IN CMDHB (SOURCE: ADAPTED FROM CMDHB 2009 P16).

	2009	2010	2011	2012
Participants	1,971	2,464	3,081	3,851
Participants as proportion of outpatient attendances	6.6%	7.8%	9.3%	11.1%

The pharmaceutical industry sponsors 85 percent of CCRep's trials, which is higher than the average for New Zealand (53 percent) and Australia (50 percent). While no one has investigated the impact of the pharmaceutical industry sponsoring a high percentage of clinical trials, there are some concerns at the '*excess dependence'* on sponsored clinical trials within CMDHB (Counties Manukau District Health Board 2009a, p6). However, the nature and costs of such dependence is not known. CMDHB projects that the numbers of patients participating in pharmaceutical industry-sponsored studies will increase by twenty-five percent per year in the future (Counties Manukau District Health Board 2009**)**. Table 1.2 reflects the impact on participant numbers. CMDHB is anticipating that, by 2012, it will have 3,851 or 11.1 percent of all of its outpatients enrolled in sponsored clinical trial. In 2015, the percentage of outpatients participating in sponsored clinical trials is expected to increase to fifteen percent (Ryan 2009).

New Zealand DHBs are not required to report on research activity, therefore, neither the extent of clinical trials activity nor the financial impact of conducting clinical trials in a publicly funded New Zealand hospital is known. This research will assist in developing a better understanding of

clinical trials in New Zealand**.** In 1990, the pharmaceuticals industry in New Zealand employed 1,000 people. This had reduced to 596 by 2004 (Watson 2006). Watson attributes this drop to the introduction of PHARMAC and other restrictive government practices, which led to considerable large pharmaceutical company retrenchment. A study by Access Economics supports this view (2003 p70).

> *Restrictive practices in the late 1990s resulted in many companies reconsidering their position in New Zealand, falling staff numbers, removal of products and withdrawal of research and development funds.*

Other sources that have linked New Zealand's declining clinical trial status with restrictive government pharmaceutical policy and regulations include Watson (2006), Australian Government (2004), and the Health Research Council of New Zealand (2002).

The pharmaceutical companies are concerned about the restrictive nature of PHARMAC policies. Sage and Jellie sum up the potential impact on central government policy (2003 p1):

> *The challenge for the Government is to find an appropriate way to balance the very tangible cost of drug procurement against the less tangible cost (but potentially huge benefit) of encouraging research and development within New Zealand.*

New Zealand has a highly regulated pharmaceuticals market (Watson 2006). The Government is the primary funder of pharmaceuticals with twenty-one DHBs administering the budget for all hospital purchases and for the community Pharmaceutical Schedule (PS). The PS budget funds prescription pharmaceuticals, across the counter medicines, special foods and ancillary devices. PHARMAC is responsible for the oversight of government expenditure on pharmaceuticals. This means they manage and negotiate cost with pharmaceutical companies on behalf of all New Zealanders. PHARMAC's goal is to obtain the best value possible in the purchase of pharmaceuticals. Medsafe manages the pre-market approval system for pharmaceuticals. Medsafe and PHARMAC work independently (Medsafe nd)

If the benefits to the economy of undertaking clinical research are greater than the costs then there may be justification for tax or other government incentives or a more competitive pharmaceutical marketplace. This has been evidenced in Australia where a 2003 review of returns on health research and development (Access Economics) led to an investment review of health and medical research followed by more favourable government policies (Australian Government 2004). Specifically Access Economics researchers find health research and

development when viewed as an investment offers 'exceptional returns'. They suggest that a strategy to obtain the most out of this investment will include developing public/private partnerships, particularly if this involves partnerships with oversees funding sources and maintaining a broad range of fundamental research areas (Access Economics 2003).

In 2010, the New Zealand government launched an enquiry into improving New Zealand's environment to support innovation through clinical trials. The major issue facing the government relates to PHARMAC, which restricts public spending on pharmaceuticals. The question is whether partial liberalisation of PHARMAC will bring economic benefits through additional clinical trials and whether this will risk significant harm to the public. The pharmaceutical industry, naturally, wants full liberalisation of PHARMAC and in exchange is promising significant returns from their increased investment in clinical trials. The current study uses BCA to assess the value of clinical trials and in doing so will inform the debate on the value of clinical trials in New Zealand.

Internationally there is growing concern about the way commercially sponsored clinical trials are performed (Angell 2004, Johns, Barnes and Florencio 2003, Wynia and Boren 2009, Sade 2009). There is a growing belief that pharmaceutical companies have too much control over clinical trials and that this leads to bias in the results. There is increasing awareness that most new drugs are just variations of older drugs and that some clinical trials are simply a marketing tool, used by drug companies, to sell more pharmaceuticals (Angell 2004). Dr Richard Horton, editor of The Lancet, cited in the House of Commons Health Committee (2005 p158) in Britain observes the pharmaceutical industries dominance in the National Health Service:

> *It provides people; it provides equipment, services, buildings, facilities and, of course, hospitality. At almost every level of National Health Service, care provision the pharmaceutical industry shapes the agenda and the practice of medicine.*

DEVELOPMENT OF THEORY AND METHOD

This study makes four important contributions to the development of theory and method; by 1) extending the application of BCA in the accounting literature, 2) enhancing value measurement in the health sector, 3) extending the application of mixed methods research in accounting and 4) further developing method in the formation of a social report. The researcher develops these

contributions through the course of the thesis before bringing them together in a final discussion in discusses in chapter 7.

STATEMENT OF REFLEXIVITY

Reflexivity is important for all researchers, no matter which methods and perspectives they use (Gilgun 2010). A researcher is reflexive when they are aware of the multiple influences they have on the research process and on how the research process affects them (Gilgun 2010). This section provides a personal statement of the researcher's reflexivity

I bring a varied and multidisciplinary perspective to this research. I initially trained as an occupational therapist and spent eight years working in psychiatric and general hospitals. This health background has enabled me to understand the hospital system in which this research has taken place but may also have influenced my interpretation. My occupational therapy training was helpful for understanding the vast amounts of medical jargon used in health settings. It influenced the way I communicated with the professional staff. My experience running groups and in particular group therapy sessions while working in psychiatry gave me the grounding I needed to run the focus groups in the study. I held a position of charge occupational therapist prior to leaving this occupation to start a family. My experience in this head of department position informed me of how and where to get information within a hospital setting which made the research process easier.

As a senior lecturer in management, I was able to utilize the students of a business environment class to gather surveys. I have been an elected member of my local community board. This experience and the networks that I established in this role allowed me easy access to the politicians used in the study. It is possible however that their knowledge of my political opinions may have swayed their responses. This statement of reflexivity acknowledges that researchers influence research processes and research processes influence researchers. The two are interconnected and have had impact on the outcome of this study.

CONCLUSION

The research question is: 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital? Value theory is interdisciplinary and discussion and debate

appears in a multitude of accounting, economic, ethical, health and sociological literature. In particular, value and accounting have historical roots, which have over time developed into a closely interwoven association. Although there is no one accounting theory that satisfactorily explains the concept of value accountants can draw on a number of theories to illuminate value and value creation. The health sector is facing challenging resource issues resulting in a need to refocus the attention of decision makers on increasing value in health care. Accountants will have a key role to play in achieving this goal. Measuring value is a difficult task and a number of approaches are available. One way to measure value is by conducting a BCA. To illustrate this form of value application and measurement, this thesis reports the results of a BCA that examines the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital.

This first chapter of this thesis presents its background, specifies the problem under investigation, describes the motivation, introduces, and presents an overview of the empirical study. Chapter 2 provides a synthesis of the literature and an examination of the theoretical foundations of the study. Chapter 3 reviews the relevant empirical studies that contribute to the understanding of the value of clinical trials and then identifies the health research outcomes classifications that can be used to model value creation. The chapter analyses the literature to appraise the background of the overall project highlights the potential benefits and costs of clinical trials and identifies knowledge gaps. Chapter 4 presents the research design and provides an explanation for the sampling techniques and data collection methods used. It describes and justifies the separate approaches to data analysis for the economic outcomes and the multiple stakeholder perceptions strands used in the study. Chapters 5 and 6 present the results for the qualitative and the quantitative phases of the study respectively. The final chapter (chapter 7) concludes by challenging a number of implicit assumptions on value held within conventional accounting. It summarises the core outcomes of the reported case study. It then examines the implications of the results for the measurement and reporting of value in future studies. It identifies the strengths and limitations of the study and ends the thesis by providing recommendations for further research.

2. LITERATURE REVIEW

As indicated in chapter 1 the research question is: 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?' Chapter 1 considers the nature of value, identifies the importance of value within the health sector and establishes the context of the case study. It then justifies the study and outlines its structure while this chapter reviews to literature and establishes its theoretical framework. The next section examines the theoretical foundations of value and its measurement. Next, the chapter reviews the literature on stakeholder perspectives on value. The conclusion of the chapter identifies and provides a brief discussion on the key concepts, which emerge from the synthesis of the literature identified in this review.

VALUE AND ITS MEASUREMENT

The concept of value raises accounting, economic, political and sociological issues, which require discussion and debate across disciplinary boundaries and community and policy-making arenas. Reviews of the management accounting literature (Ferreira and Merchant 1992, Abernethy, Chua, Luckett and Selto 1999, Chapman, Hopwood and Shields 2006, 2007 and 2009) and the social accounting literature (Barrett and Scott 2008 and Deegan 2002) show that no single accounting theory fully explains the nature of value; therefore, this section draws on a number of theories to provide a frame of reference. First, the section reviews the literature on the concept and theory of value. Next, it develops an understanding of value as it applies to the healthcare sector. It then identifies the role of accounting in measuring costs in healthcare and reviews economic methods for measuring value. This section concludes by considering merging perspectives on value.

THE CONCEPT AND THEORY OF VALUE

A holistic notion of value informs the current empirical study. The study identifies value creation and value capture in its widest form and as perceived by multiple stakeholder groups. Although often erroneously merged, value creation and value capture are different concepts (Makadok and Coff 2002, Toms 2010 and Bowman and Ambrosini 2000, Lepak et al. 2007). 'Value creation'

is the value gained directly from a project, whereas 'value capture' is what the organisation gains indirectly when that value is retained (Birmingham 2006 and Lepak et al. 2007).

There is considerable overlap between theories in accounting literature, with individual theories often providing slightly different insights into the topic in question (Gray *et al*. 1995). Recently scholars have used more than one theory to provide useful explanations in their analysis of '*particular managerial actions'* (Deegan 2002). They reason that because all theories make simplifying assumptions, no single theory is ideal for understanding or explaining every aspect of reality (Holcombe 2011). With reference to this view Parker (2005 p849) states,

> *…pluralism in theoretical lenses and methodologies applied to common research problems can yield incremental and accumulating insights that are enriched by both commonality and difference. All are valuable. That Holy Grail, the all-encompassing unitary explanatory social and environmental accounting theory, is not only a mirage, but cannot deliver the richness of insights we need in this complex and changing field of research and action.*

Using different theories to analyse a phenomenon can broaden understanding because the assumptions that one theory may make can eliminate insights that can be gained by using different assumptions and theoretical approaches (Holcombe 2011). Mindful of these advantages, this study takes a pluralistic approach, using different theoretical frameworks and points of view.

Defining value can be highly subjective. Blumenfeld, (1961 p315) states that value involves:

> *1) an object (person, group, thing, process, behaviour, idea);*
>
> *2) a special characteristic of the object as positively or negatively "valuable"*
>
> *3) a being for which the object is or becomes consciously valuable from one or another viewpoint;*
>
> *4) a process by means of which such a "valuation" is achieved and*
>
> *5) certain situational conditions, in which the process takes place*.

Hartman (2011) reports that value theory began in classical Greece when Aristotle distinguished between value in use (utility) and value in exchange (price). Economists in the 1800s posed the question of 'why water, which is more useful than diamonds, has a lower price than diamonds' (the diamond-water paradox) as a means understanding the role utility plays in the demand price of a good (Hartman 2011). Water has utilitarian value but no exchange value while diamonds have exchange value but no utilitarian value (Winfrey, 1993). From this basis, scholars identified

that the value of a good is the result of its utility and scarcity, not its intrinsic value. This means that the value of a good is determined by the quantity supplied and demanded (Pack 2010).

Two theoretical paradigms dominated economic theory for more than 100 years: the classical political economy and the neo-classical economics of marginalism. From these two competing forces have come two conflicting theories: the 'Labour theory' and the 'Marginalists theory' (Tinker 1980, Bryer 1994 and Sørensen 2002). Karl Marx was an exponent of the 'Labour theory' of value, held also by Adam Smith, and David Ricardo, as well as some other early 19th century political economists (Pack 2010). Marx's labour theory of value states that the value of an object is the result of the labour expended to produce it. Therefore, the more labour hours that go into producing an object the more it is worth (Pack 2010). Commodities are exchanged in the ratio of the quantities of labour required to produce and then market them with any surplus value being profit (Bryer 1994). Commodity value is equivalent to the value of the quantity of socially necessary labour consumed to produce it (Dobb 1973).

Whereas the labour theory of value treats labour, and therefore the foregoing of leisure, as the cost (or value) of anything, marginalist theory views labour as a cost but not the only cost. The marginalist theory switches the focus from the average value to the value of the marginal item (Hicks 1946; Bryer 1994; Tinker 1980). Individuals receive utility by using, holding, or consuming a good. However, the utility derived from each additional unit of a commodity- the marginal utility- is worth less and less to the individual. For example, the first food an individual consumes when acutely hungry is more valuable than the last (Tinker 1980). The theoretical foundations of accounting derive from marginalist theory and most accounting practices depend on marginalist thought (Bryer 1999). For example, marginalist theory is evident in asset valuation and financial standard setting (Hicks 1946; Bryer 1994; Bryer 1999). In addition, economists use marginalist theory to evaluate the present value of future cash flows (Bryer 1999).

Value is an elusive concept, which can be difficult to measure (Bowman and Ambrosini 2010). It is subjective and may hold '*different meanings for different people, or at different times, different meanings for the same person'* (Hiltner 1975 p1). Value can therefore mean different things to different organisational stakeholders (Bowman and Ambrosini 2010). Bourguignon, (2005) subdivides 'value' into three clusters: (1) measurement value, (2) economic value and (3) philosophical value. Measurement value is comparable to the measure or approximate

quantification of an element in a hierarchically structured series. Economic value includes both usage value (the social utility of a commodity) and exchange value (the relation between supply and demand), (Pack 2010). Usage value comes from the properties of products and services that provide utility. Exchange value is a monetary amount exchanged between the firm and its customers or suppliers when usage values are traded (Bowman and Ambrosini 2010).

Philosophical value is a property of objects, including physical objects as well as abstract objects, representing their degree of importance or worth.

Philosophical value can be sub-classified into subjective and objective values. Subjective value identifies worth as the wants and needs of a subject (Bourguignon 2005). It involves personal opinions and feelings rather than on facts. In contrast, objective value is grounded in fact. Objective value includes both intrinsic value and instrumental value. Intrinsic value is contained within and is based on social utility (Bourguignon 2005). Instrumental value is the value associated with meeting a specified goal or purpose (Bourguignon 2005).

Management accountants often investigate the strategic process of value creation within organisational activities (Lepak, Smith and Taylor 2007). Bourguignon (2005 p353) regards value creation as a strategic activity:

> *The 'value' which is referred to in value creation is not the usual accounting 'value'. Value creation is not first and foremost an accounting, but a strategic concept. Management accounting contributes to its implementation—as it serves any other strategic objective.*

Bourguignon (2005) identifies two key approaches to value creation in use within the management accounting literature (1) that associated with customer value and (2) that associated with shareholder value. He observes that although customer and shareholder values both pursue 'value creation' as the main strategic goal for the organisation, they approach this goal in radically different ways (Bourguignon 2005 p364). Customer value stems from Porter's view that value results from customer needs (Porter 2008 p3):

> *Value is what buyers are willing to pay, and superior value stems from offering lower prices than competitors for equivalent benefits or providing unique benefits that more than offset a higher price.*

Customer-value oriented management accounting therefore focuses on the need for managers to take a systems approach and to focus on value, not only costs, although over time some costs

may transform into value (Town 1998). There is a clear relationship between cost value and price (Allen 1996 p32):

> *When we acquire or develop something, it is in the belief that its value-- what it is worth to us is greater than its cost. When we sell something, it is in the belief that the price we get for it is greater than its value to us.*

Bititci, Martinez, Albores and Parung (2004) refer to customer value as external value where value equals satisfaction. In the current study, trial participants are considered customers, as they are the end users of the service provided.

Shareholder-value oriented management, often-referred to as value-based management, is based on the idea that the only reliable measure of corporate strategy is whether it creates economic value for shareholders (Rappaport 1986, Bititci, Martinez, Albores and Parung 2004). This orientation was made popular in the 1990s by researchers such as Ronte (1999) and Condon and Goldstein (1998) and Booth (1997). The pharmaceutical companies in the current study have a goal of maximising their shareholder value.

Accounting literature usually presents stakeholders as either shareholders or customers (Bourguignon 2005). Other discipline areas, however, extend the range of stakeholders they consider and may make distinctions between the values created at an individual, organisational or societal level (Lepak et al. 2007). The accounting literature also fails to consider value creation within the not for profit sector. Birmingham (2006 p11) suggests a possible reason for this:

> *The concept of value in the for-profit sector is often, and appropriately, defined as revenue increase, cost decrease or some other interaction that improves an organization's financial status. Value in the non-profit center, where profit is not the motive, is more challenging to define and measure*

A clinical trial may create value by developing a new drug. The DHB may then capture that value when the staff having seen the new drug being developed start prescribing it to their patients. Organisations may create value at one source and capture it at another as Lepak et al. (2007 p2007) explain,

> *.... although an individual may create value by developing a new way to perform a particular task in the workplace, other parties, such as organizations or even societies, may benefit more from the value that is created than does the individual creator.*

The current study identifies both value creation and value capture through an analysis of benefits and costs from multiple perspectives.

Murphy and Topel (1998) classify value as either public or private. Public goods create public value. There is no limit to how many people can consume them. To calculate public value economists use both the current and expected future populations benefit from use of the public good (Murphy and Topel 1998). Private value is the value, which is available to individuals. To calculate private value an assessment is made of the individual benefits over their lifetime (Murphy and Topel 1998). Clinical trials are likely to produce both public value (for example, vaccinations limiting the spread of disease) and private value (for example, improved individual health). In the current study these values will be recorded as benefits and costs to the various stakeholder groups.

Estimating the relative contributions or rates of success of industry-sponsored as opposed to government-supported research is difficult (Montaner, O'Shaughnessy, and Schechter 2001). Many treatment innovations have emerged from commercially sponsored clinical trials however, the contribution of government and non-commercial sponsorship in the early stages of these innovations is not always obvious. Zycher et al. (2008) emphasise the interdependence of public and private sector contributions to the discovery of new drugs. They argue that public- and private-sector research complement each other and are equally necessary for new drug development although the balance between public and private contributions varies from country to country. The interdependence of public and private sector contributions to the discovery of new drugs is also recognised by Reichert and Milne (2002 p19):

> *The basic research that underlies new therapeutic compounds is a combination of publicly available biomedical knowledge and basic research conducted by firms. There is a high degree of complexity and creativity in the process of drug discovery. Nevertheless, there is a progression in research and learning. To the extent that firms monitor and use publicly available medical knowledge in their research, they can begin the process of drug innovation with something other than a 'blank chalkboard'.*

Woolf and Johnson (2005) argue that society's large investment in drug development consumes resources that are needed for improved delivery of health care. They suggest that although pharmaceutical companies are concerned about the general health of the population they are ultimately accountable to their shareholders. Despite this, they suggest that decision makers in

health systems should retain a global perspective and consider which health care investments serve the greater good for the population. Woolf and Johnson (2005 p545) argue:

> *Health, economic and moral arguments make the case for spending less on technological advances and more on improving systems for delivering care*.

Positive stakeholder relationships can result in value creation for the organisation (Wheeler Colbert. and Freeman 2003, Mills and Weinstein 2000). Svendsen (1998) observes that the locus of value creation often lies outside the boundaries of a single firm. In addition Post, Preston and Sachs (2002 p8) note that value can also be created for stakeholder groups '*Corporations create wealth in many different forms—earnings for investors, compensation for employees, benefits in excess of costs for customers and others.*' Value creation also occurs when organisations collaborate in partnership or alliances (Doz and Hamel 1998). Conducting clinical trials is a collaborative activity involving the health board and the sponsoring organisation. However, to be successful they need the co-operation of many other stakeholder groups. These additional stakeholder groups contribute to value creation and value capture. The current study investigates the value created from seven stakeholder groups involved in clinical trials. The literature review reveals no other study that has investigated a multiple stakeholder approach to value creation.

Social accounting has grown out of an awareness of the need for responsibility and accountability to stakeholders for organisational performance (Gray, Dillard and Spence 2009). It includes both the valuation of social benefits and costs that are quantifiable in money terms as well as those social impacts that are not so easily quantifiable (Boyce 2000, Este 1976, Gray et al. 1996). In general, social accounting scholars contend that accounting information should be readily accessible so that all stakeholders are free to share decision-making responsibility in society (Medawar 1976; Gray 2002, and Barrett and Scott, 2008). Social accounting research extends corporate stewardship beyond its focus on shareholders to its many stakeholders (Barrett and Scott, 2008).

There is no one accepted theory for social and environmental accounting research (Deegan 2002). Some social accounting theorists draw on the systems orientated perspective to inform their research (Barrett and Scott 2008). The systems orientated perspective assumes an entity influences and is influenced by the society in which it operates (Deegan 2002). This perspective is useful in the current study as it allows opportunities to '*focus on the role of information and disclosure in the relationship(s) between organisations, the State, individuals and groups*' (Gray

et al. 1996 p45). Two key theories, which adopt a systems orientated perspective, are legitimacy theory and stakeholder theory. Stakeholder theory and legitimacy theory are overlapping '*perspectives on the issue which are set within a framework of assumptions about political economy'* (Gray *et al*. 1995 p52). Using Deegan's (2002 p292) words, political economy theory considers:

> *Society, politics and economics are inseparable and economic issues cannot meaningfully be investigated in the absence of considerations about the political, social and institutional framework in which the economic activity takes place.*

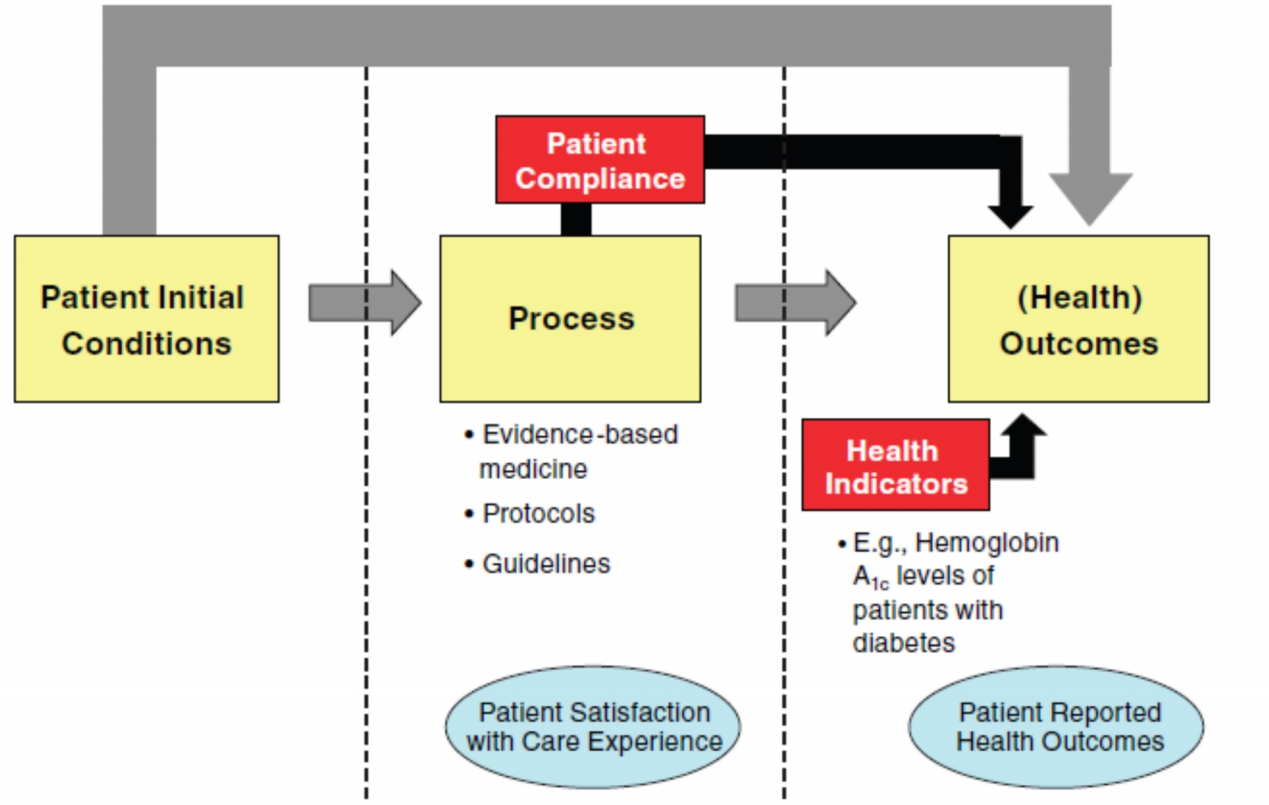
Emerging from the literature on approaches to understanding value is the illusive nature of the concept of value. Creating a common approach to defining and assessing value in health care is becoming increasingly important given the current rising expenditures on health care and the turbulent economic environment (National Research Council 2010).

VALUE IN HEALTHCARE

Porter (2010) considers that the key aim for the delivery of modern healthcare is value. Porter (2008 and 2010) develops an approach for improving value in health care. As Porter's framework is significant to the way value is conceptualised within the health sector it is explained in detail here. This section draws from Porter (2008), Porter (2010), Porter and Teisberg (2006). Increasing value is a goal that unites stakeholders and is central to achieving improvements such as better population health, increased health access and improved health equity, safety and efficiency (Porter 2010).

Porter (2008 p162) defines value as a '*measurement of patient health outcomes per dollar expended to achieve those outcomes'*. The outcomes in the health system are total patient health outcomes rather than the services delivered at a clinical location. He defines value around the customer, and not the supplier and measures value by outputs, not inputs. The cost of achieving outcomes is the total cost of all the inputs involved in the entire treatment process rather than the cost associated with any one clinician or for any particular treatment or episode. Value is improved when '*equivalent outcomes are achieved at a lower cost, or better outcomes are achieved at comparable (or lower) cost'* (Porter 2008 p163). Outcomes and costs work together.

FIGURE 2-1 MEASURING VALUE IN HEALTH CARE (SOURCE: PORTER 2008 P164).



Improving outcomes will reduce the need for additional care and therefore decrease cost. Patient value not cost containment is thus, justified as the prime goal in the health sector (Porter 2008).

Value is largely unmeasured in today's health system (Porter 2008). The first step in measuring value is to measure health outcomes. Medical conditions can produce numerous health outcomes that combine to determine value. Health outcomes may include survival or death, the nature and speed of the recovery process or the sustainability of the cure and may involve trade-offs between individual outcomes.

Porter (2008) observes that one key mistake in measuring outcomes is to confuse processes and structures such as protocols, guidelines, and practice standards with outcomes. Structures and processes may indicate outcomes but they are not always accurate (Porter 2008). In addition, Porter (2010) suggests patient satisfaction with their treatment may not always result in improved patient health outcomes. Figure 2.1 illustrates Porters model for measuring value in health. It shows the relationship between health process and health outcomes.

The structuring of healthcare does not always allow alignment across the organisational boundaries of health delivery. One single intervention seldom determines patient outcomes, but health outcomes are often measured by the productivity of one department, clinician or treatment. This provides an incomplete understanding of patient outcomes and does not measure total health value. '*What is measured is what is easy to measure, rather than what matters for outcomes*' (Porter 2008 p168). Porter (2008) considers that value is the responsibility of all clinicians involved in determining the outcome.

Outcomes can be difficult to define and isolate. The health outcomes of interest to the patient may not be the same as the outcome of interest to clinicians and researchers (Gray 2011). Although Porter defines value in terms of the relationship between costs and outcomes this is not a widely recognised definition among all stakeholders (Quintiles 2011). This lack of consensus on the meaning of value in healthcare influences the questions used in the multiple stakeholder perceptions strand of the current study.

Some health services (for example end of life care) have very high costs, the health outcomes are poor because it is end of life care. Using Porter's approach end of life care has low value, however, having the right kind of end of life care is of high value to patients and their families. In this instance from the patient's perspective Porter's focus on cost and outcomes is insufficient. Gray (2011) takes a more comprehensive approach when he identifies three key factors, (1) hotel amenities, (2) interpersonal and (3) technical /clinical, that influence patient experience. The hospitals hotel amenities include the cleanliness and state of repair of the buildings, the car parking and the food. The interpersonal experience includes the politeness and respect shown to patients. The technical / clinical aspect relates to health treatment outcomes. To understand how patients perceive value in healthcare requires a consideration of all three aspects of patient experience. The current study incorporates process as a consideration when measuring value. The study design measures costs, perceptions relating to process and health outcomes. Value, therefore, becomes a combination of costs divided by process and outcome. Measurement of value in health care is an increasingly important goal. As the meaning of value changes as the stakeholders change, methods of estimating value need to take into account the significance of perceptions and perspectives and the importance of the relationship between quality, resource use, and cost (National Research Council 2010).

COST MEASUREMENT IN HEALTH CARE

Cost is among the most pressing issues in health care, and for many years, accountants have led the way in efforts to control them. Early health care accounting was limited to developing accounting systems (Bloomfield, Coombs, Cooper and Rea 1992, Rea 1994). '*Hospitals and health management had invested lightly in the accounting craft, in part because health care had not been perceived as primarily an economic phenomenon*' (Hopwood 1990 p16). From the 1950s, to 1980s a department-based costing system was favoured expressing expenditures at highly aggregated functional levels (Rea 1994). Hopwood 1992, Bloomfield *et al*., 1992 point out that resource management was the sole responsibility of the medical profession and according to (Rea (1994 p87):

> *rights of clinical autonomy meant the work of doctors could only be assessed by other members of the profession, according to whether it was within accepted standards of treatment and ethics. Decisions to treat, over forms of treatment, and over treatment duration remained relatively free of accountability outside the profession.*

The need to tackle resource allocation and health sector accountability gained prominence as health care costs increased (Broadbent and Guthrie 1992). Health sector accounting at this time was primarily concerned with its treasury function rather than the provision of information for managerial decision-making (Hopwood 1984). Attempts to restrain expenditure through complex planning and costing systems fell on the shoulders of the accountant (Rea 1994).

Internationally the health sector was a focus for reform in the 1980s as escalating public expenditure brought pressure for cost savings, performance improvements and more equitable delivery (Broadbent and Laughlin 1998, Lowe 2000 and Cordery, Baskerville and Porter 2010). Lawrence, Alam, Northcott and Lowe 1997 p668 observe that accountants played an important role in these changes:

> *Institutional rearrangements and new funding mechanisms introduced by government were intended to affect the systems of accountability in hospitals, and the new commercial orientation brought the need for better technical accounting systems.*

Health care accounting emphasised cost control and containment (Preston, 1992) which involved the definition, measurement and costing of health service outputs (Jones 1999). Effectiveness and efficiency grew in importance, because funding was made available only to those services

that produced positive results at a reasonable cost (Gray 2011). Calls to improve efficiency in the health sector were accompanied by the reorganisation of accounting information (Hopwood 1984 and Robson 2008), and increasing debate over the impact of accounting within health care reforms (Broadbent, Laughlin and Read 1991 and Preston 1992). Chua and Preston (1994 p15) explain the importance of accounting during this period:

> *Accounting-led initiatives, however are not merely techniques to control costs and promote efficiency, as proponents argue; they have a profound constitutive role to play in shaping medical practice, the provision of health care and the experience of the patient as well as circumscribing the ground on which we are able to talk about healthcare.*

The public often assume that accountants are fully responsible for what is occurring in their public hospitals (Lawrence *et al*., 1997). Lawrence *et al*., 1997, p670 note that initially during the early 1980s there appeared to be a conflict and power struggles between clinical staff and accountants, as reflected in this extract from an interview with a General Manager Finance, 23 June 1994:

> *A finance manager recalled the attitude of clinicians to the financial management reforms. During a meeting at a regional hospital to discuss a move towards clinical budgeting, a clinician stood, moved towards the door, and before leaving, said: "Mr X, if you think that money will ever determine what decisions I make, then you are mistaken."*

Nevertheless, as the realities of the economic environment became evident accounting became a more accepted part of life in the health system (Lawrence *et al*., 1997, Chua and Preston 1994). In the late 1990s Lawrence *et al*., (1997 p 679) report:

> *There has been an integration of clinical and business language, and a new emphasis on accounting and economics has become evident in the health sector, and with it a new way of acquiring access to resources.*

A recurring issue debated within health sector accounting is, '*What should the cost-unit be?*' (Robson 2007 p353). The initial preferred unit was cost-per-bed but as health specialisations grew, a search for more precise costing units became critical (Jones 2001 and Robson 2007). This created '*a gradual evolution of cost information, an increasing number of cost-units and more intricate allocation processes*' (Robson 2007 p353). Currently many costing units are used in the health system (Robson 2007 p353),

> *A reluctance to drop previous costing information following the adoption of new data, resulting in a multi-layered approach, for example cost-per-day continued when departmental data were created and departmental information continued after specialty costing data* (Robson 2007 p353).

This can make the data collection more difficult and may contribute to problems of work overload and inaccuracy (Robson 2007). The empirical study described in this thesis draws on a number of different budget categories to identify costs. Porter (2008) advocates that the cost of the entire health care process should determine the true costs of delivering health care therefore overall value. This includes any separate facilities such as rehabilitation centres and the costs borne by the patient or within primary care. From a practical point of view, this means dividing budget sheets up into programme expenditure categories such as infectious diseases, cancers and tumours or blood disorders to compare programmes of treatment and efficiently allocate resources between programmes. The current study compares the cost of treatment for participants and control groups in an attempt to measure the total cost of care but due to difficulties in obtaining the cost data only key costs such as pharmaceuticals and laboratory costs are compared.

Accounting in the health sector has been in a process of constant change and renewed focus (Robson 2007). Gray (2011) predicts the focus for the next era in the health sector will be on value Gray (2011 p1):

> *21st century healthcare will be dominated by patients, outcome and value, because the challenges facing 21st century healthcare in every society are massive and growing*.

Changes driven by communities will create health services that are patient centred, are safe and effective and produce greater value from the resources used (Gray 2011). Accountants and economists will both be important in driving the changes.

ECONOMIC METHODS OF MEASURING VALUE

Like many countries, New Zealand faces high demands on its health care system and has limited resources to meet this demand. The objective of economic evaluation in health is to compare value in health programmes and treatments even if they are quite different (Gold et al. 1996). Economics acknowledges the scarcity of resources and provides suggestions on how to best

organise society in a way that makes the most efficient use of those resources (Samuelson and Nordhaus 2001). Central to this theory is the concept of 'opportunity cost'; if we use resources in one way there is an opportunity forgone to use those resources in some other way (Drummond, O'Brian, Stoddart and Torrance 2000).

Economic scholars commonly discuss the concept of value, and, using Boulding's words (1956 p1), **'***The word value occurs in economic writing with high frequency, the frequency of meanings being about as great as the frequency of occurrence***'.** The traditional economic approach to value in health aims to maximise health gain subject to budget constraint, by ranking treatments according to the results of economic evaluation. Economic evaluation assesses whether one particular intervention is worth undertaking compared to another intervention (or compared to doing nothing). Economic evaluation provides a basis for identifying the value of clinical trials. Value is either positive or negative (Wheeler *et al*., 2003 and Blumenfeld 1961). Both positive and negative value is important in this study due to the controversial nature of clinical trials. A benefit cost analysis is one method for identifying both positive (benefits) and negative (costs) value created by the process of clinical trials. Baum (2010 p1) poses a logical argument as to why costs and benefits hold value:

> *That costs and benefits hold (or at least are considered to hold) value should be clear: costs hold negative value; benefits hold positive value. To deny that costs and benefits hold value is to deny that CBA has any meaning as an evaluative procedure.*

Lenman (2000) also identifies BCA as a tool to determine value. BCA establishes preferences during the evaluation process and then uses them to determine the value of outcomes. Individuals may have different perspectives that influence their judgement of value and as such, inform the BCA. Whittington and MacRae (1986 p675) write:

> *Whatever its theoretical elegance, cost-benefit analysis is essentially an ethical procedure for comparing elementary values, including intrapersonal comparisons among valuations of various goods; interpersonal comparisons; comparisons over time; and comparisons of the values of various alternative uncertain events.*

The current study next reviews several methods of economic evaluation including cost minimisation analysis (CMA), cost consequence analysis (CCA), cost effectiveness analysis (CEA), cost utility analysis (CUA) and benefit cost analysis (BCA). Table 2.1 provides a summary of the key differences between them. Oakes et al. (1994 p18) suggest that although

each type of evaluation places a different emphasis on the way they compare benefits and costs and each may be better suited for different aspects of the health care system, they share a common objective:

> *to create a calculus of health care where outcomes can be objectively defined and measured, and where true costs can be identified and counted. This calculus can then be used to rank medical activities and prioritize health care expenditures.*

TABLE 2-1 COMPARISON OF APPROACHES TO ECONOMIC EVALUATION

Analysis Method	**Economic School**	**Unit of cost**	**Unit of Outcome**
Cost minimisation	Economic school	Dollars	Regarded as equal
Cost consequence	Decision-maker	Dollars	Table of multiple physical units
Cost effectiveness	Extra welfarism	Dollars	Ratio of physical units of single effect for example cost per life year gained
Cost utility	Extra welfarism	Dollars	Ratio of physical units of multiple effects for example cost per QALY
Benefit cost	Welfarism	Dollars	Dollars
Analysis Method	Economic School	Unit of cost	Unit of Outcome

Economists use CMA when the consequences of two different health interventions are similar but the costs are different. As CMA measures and compares input costs in isolation (it assumes outcomes to be equivalent) the types of interventions that can be evaluated with this method are limited; in particular, it can be used only when outcomes are certain or subject to the same degree of uncertainty (Drummond, O'Brien, Stoddart and Torrance 2005).

CEA measures the effects of health programmes in terms of overall costs for some additional health gain (Sorensen and Grove 1977); that is, it measures technical efficiency (Drummond et al. 2005). Technical efficiency answers the question of 'how?' In other words, given a specific objective, how can we meet this objective at the least cost? CEA uses the most appropriate physical units, for example, life years gained or additional heart problems diagnosed. This leads to a major disadvantage of CEA in that it generally has difficulty in coping with more than one output (Mooney 2003). CEA does not attempt to value the benefits gained in terms other than the

cost, preferring to present analyses in terms of a single ratio for example $50 per one point of blood pressure reduction (Drummond et al. 2005). The choice of the comparison treatments in calculating a CEA ratio is imperative. An option looks cost-effective when compared to a sufficiently cost-ineffective alternative. In addition, problems arise in comparing different study's if the comparison program is not the same in each case. When this occurs and comparisons are non-standardised and researchers fail to justify the choice of comparator(s), interpretations across treatments are difficult (Drummond, *et al*. 2005).

Using CCA economists identify the impact of treatment alternatives on lifetime resource use and costs and health outcomes and present these in a tabular format (Mauskopf, Paul, Grant and Stergachis 1998). This may include costs for specific healthcare service use and productivity losses and benefits such as quality-adjusted life-years (QALY) gained (see discussion below). The decision-maker may use selected items from the CCA to compute composite measures of the value of the intervention. The aim is for the impact of the health intervention to be as comprehensive and transparent as possible while allowing the decision-makers to obtain the information they need (Mauskopf et al. 1998). A CCA is therefore an analysis that makes the fewest assumptions and allows the greatest freedom to decision-makers (Canadian Coordinating Office for Health Technology Assessment 1997).

A CUA adjusts the outcome units in a CEA by 'utility scores'. The utility scores show the consequences of health programmes in terms of overall health improvement and show how much it costs for a unit of additional utility gain (Mauskopf et al. 1998). One example of this is QALY, which allow the decision maker to consider changes in both quantity and quality of life (Gold et al. 1996). Like many other evaluation methods CUA assists in allocative efficiency by providing a framework for deciding which programmes should take priority but CUA differs from other methods as it avoids the controversial task of assigning monetary value to outputs.

One significant weakness in CUA for health evaluation is that CUA assumes that increasing QALY is the only objective of health care and therefore does not take into account intangibles such as information, equity of access and autonomy (Mooney 2003; Mooney and Lange 1993).

BCA addresses the concept of allocative efficiency (Drummond et al. 2005) and is described by Obeng (2008 p1) as a '*necessary, objective means to justify investment*'. BCA answers the question of whether something should be done and how much should be done (Boardman, Greenberg, Vining and Weimer 2006). A BCA converts benefits and costs into monetary terms

and compares them. BCA differs from CUA in that the 'utility scores' used to evaluate costs and benefits are dollars which, in turn, reflect opportunity costs or willingness-to-pay. Willingness (and ability) to pay is the foundation of the economic theory of value. The idea is that if something is worth having then it is worth paying for (Drummond et al. 2005). Techniques used to value willingness-to-pay in the health field are criticised for two main reasons (Cookson 2003). First willingness-to-pay methods are under-sensitive to the magnitude of benefits which results in increased valuations of interventions that generate small benefits and second willingness-to-pay methods increase informants' valuations of interventions about which they are asked relative to those about which they are not asked. A BCA generally produces one figure that represents the difference between benefits and costs. Different inclusion or exclusion criteria for benefit and cost elements in BCA can dramatically affect the net benefit and thus the ranking of interventions. Decision makers use this figure to decide what should be done (Drummond 1987). They use three principles: (1) do only those things where benefits exceed costs, (2) decide on benefits and costs on the broadest of social canvases and (3) The value placed on the benefits and costs should be decided by those advantaged and disadvantaged by the activity (Mooney 2003).

PHARMAC (2005 p15), however, warns that using BCA in health studies is difficult particularly in terms of comparing treatments that improve the quality of life with those that save lives and in placing a dollar value on health benefits. Concerns also arise over the measurement of costs, particularly opportunity costs (Rafety 1998), that BCA '*fails to take into account many subjective values associated with health and life that are not captured by earnings alone*' (Drummond 1987 p607) and that BCA if used alone is unacceptable in most social service climates (Hunt and McEwen 1980). Sound priority-setting decisions can be made only if economic evaluation studies document which benefits and costs are included.

Lenman (2000) takes a wider view of BCA than that generally identified in the economics literature, insisting that it is a mistake to consider BCA as a single evaluation technique. Instead, it is a diverse genus of such techniques. Adler and Posner (2006) suggest BCA is more than an assessment of monetised benefits and costs and extend their definition of BCA to include evaluation of values that have different dimensions or qualities. The BCA therefore becomes a process of '*intuitive balancing*' the positive and negative consequences of an action (Adler and Posner 2006 p79).

This approach resolves the issues associated with monetising values and is the approach adopted in the current study. The current study includes both quantified and qualitative information in the analysis of benefits and costs. The comparative treatments are the treatments of those involved in the clinical trial and their case matched controls who receive standardised care. Accompanying qualitative data embrace a wide range of benefits and costs.

There are three economic approaches to resource allocation: (1) welfarism, (2) extra welfarism and (3) decision-making (Carter 2001). Each of these approaches has its own set of tools and evaluation methods. Welfarism acknowledges the concept of user satisfaction and gives primacy to individual utility including preference and consumer sovereignty (Carter 2001). It follows the 'Pareto principle' that individuals are the best judges of their own welfare and that if I make one person better off without making another worse off, there is a global improvement in welfare (Coast, Smith and Lorgelly 2008). A less restrictive interpretation of the Pareto principle suggests that global improvement will occur if individual(s) who are better off can compensate those who lose are worse off and still be better off (Hicks 1939). Welfarism provides the theoretical foundation for benefit cost analysis.

The term 'extra welfarism' derives from Sen's (1989 and 1982) studies on functioning and capability. Extra welfarism rejects the sole focus on utilities of individuals found in welfarism and instead extends the focus to other effects, which influence efficiency. Extra welfarism provides a theoretical basis for cost utility analysis and for using QALY in economic evaluation. QALY, discussed later in this chapter, are used in the current study.

Recently Amartya Sen's theory of social choice (Sen 1979 and 1982) has emerged as an alternative to standard economic frameworks for constructing meaningful measures of social welfare (Clark 2006). Sen's approach originates from the concept of human capability and freedom (Clark 2006) which Wallace (2004 p6) summarises in the form of a question:

> *The fundamental question is whether—and, if so, in what way—preferences for society as a whole can consistently be derived from the preferences of its members? The answer is crucial for the feasibility of ranking, or otherwise evaluating, different social states and thereby constructing meaningful measures of social welfare or helping public decision making.*

The open nature of the questions asked in the current study will allow stakeholders to identify freedom of choice as a benefit should they wish.

Sen advocates that public policy focus more on people's political empowerment and less on the provision of public services (Fukuda-Parr 2003). Chalkidou, Culyer, Naidoo, and Littlejohns (2008 p 445) observe that it is proving challenging to operationalise this concept:

> *Even more challenging, where 'choice' is pursued as a key policy priority, is the question of how cost- effectiveness analysis ought to take account of consequences whose essential character lies in the availability of options from amongst which people may choose rather than (or, as well as) the consequences of having selected from amongst them. How ought this 'option demand' (Weisbrod, 1964) be measured, valued and compared with health gain?*

Challenges to the individual utility principles of welfarism and to the ethics of QALY by health economists have led to the development of the decision maker school (Williams 1972). The 'decision-maker' school "contrasted the welfarism with its embodiment of 'individual sovereignty' with one in which 'decision-makers' were the source of values in public decision-making" (Brouwer, et al. 2008 p331). User considerations arise from an effort to ensure that the decision making process must respond to the particular needs of health care decision-makers. The decision-maker approach thus is consistent with the use of cost-consequence analysis. Carter (2001 p58) provides the motivation for using the decision-maker approach:

> *When the decision-maker is the government or a government authority, the perspective can be considered 'societal' in the sense that governments are assumed responsible for making decisions in the public interest. The government decision-maker is entrusted with the task (via the democratic political process) of making choices on behalf of the general public, and the trust implies the formation of objectives on their behalf, and importantly, the reflection of societal ethical values.*

The decision maker approach therefore elevates the status of the decision makers commissioning the analysis and provides a focus on the decision-makers perceptions of societal objectives (Weinstein and Stason 1977). Using this approach, however risks being perceived as the government having too much control over the activities of private citizens. A decision-maker approach is used to establish clinical trials in New Zealand public hospitals. By allowing stakeholders to identify their perceptions of the cost and benefit of clinical trials, the current study will be able to identify the success of this approach to be representative of the views of New Zealand society.

MEASURING THE VALUE OF LIFE.

Traditionally the benefits of healthcare were measured by the number of life years added (Gray 2011). This led to a focus on length of life as a goal of health care. Any extension of life can be regarded as beneficial, however because some life-saving treatments are unpleasant, the extended life is full of pain and discomfort, while other treatments may not save lives but will considerably improve the quality of life of the patient. Rosser and Kind (1978) identify health as a function of both quantity of life (mortality) and quality of life (morbidity). They develop the Quality Adjusted Life Year (QALY) as a measure of the value of health outcomes. The QALY combines the value of length of life and quality of life into a single index number. It assumes that a year of life lived in perfect health is worth 1 QALY (1 Year of Life × 1 Utility Value = 1 QALY) and that a year of life lived in a state of less than this perfect health is worth less than 1. QALYs combine with medical costs to produce a common denominator of Cost/QALY (Gold et al. 1996). QALYs therefore offer the possibility of carrying out cost effectiveness analysis and thus provide the information needed to make efficient decisions. In New Zealand PHARMAC uses QALYs, but also considers cost along with eight additional criteria when purchasing medicines at a national level (Gray 2011). The current study uses QALY because universally it is the best method available for measuring and comparing the health effects of varied interventions across diverse diseases (Gold et al. 1996).

Economists have used a number of techniques to assess the value of a QALY including approaches based on productivity and approaches based on willingness-to-pay (Boardman et al. 2006). Both of these methods have limitations (Ramsey 2008). Productivity measurements value the years of life lost from the workforce but ignore the value of unpaid work (Ramsey 2008). Willingness-to-pay surveys can overestimate values when compared to actual consumer choices subject to a budget constraint (Brown, Champ, Bishop and McCollum 1996). Although QALYs provide an opportunity to solve the problem of measuring health care outcomes, they suffer from a number of serious problems. Sinden (2004 p198), for example, argues that such valuing lacks authenticity:

> *We would never offer a friend a cash payment to "compensate" her for cancelling a lunch date, because we view friendship as simply incommensurable with money. Nor would a pet owner consider the "opportunity costs" of not eating her pet or not selling it for laboratory experiments. Similarly, many people balk at the prospect of attaching a*

> *dollar figure to the loss of an endangered species, the destruction of a pristine natural area, or the loss of a human life because they view these values as simply incommensurable with market commodities and thus not measurable along a monetary metric.*

Critics associate QALYs with rationing (Neumann 2011), a controversial process which includes ranking clinical procedures and therefore who will or will not receive treatment. Allocating health funds on QALY does not take into account equity issues such as the overall distribution of health states. For example, many would argue that interventions that help the most vulnerable populations, such as children, should be favoured regardless of whether these options are efficient from a QALY optimising standpoint (Neumann 2011). However, QALY supporters contend that since health care resources are inevitably limited, QALY enables allocation of scarce resources in the way that is approximately optimal for society (Gold et al. 1996). Kind, Lafata, Matuszewski and Raisch (2010) suggest the controversial nature of QALY stems from how and when QALY are used. They feel there are merits in the use of the QALY in decision-making concerned with resource allocation within patient populations, but there are boundaries to the practical usefulness of this approach at the clinical level. They state (2010 p27)

> *The use of the QALY as a health outcome measure for groups of patients is fairly clear for payers, managed care, and governmental organizations who seek to make decisions that maximize the value of health-care spending in terms of health outcomes achieved through the most efficient use of limited resources. Nevertheless, the importance and need to bring QALYs into the wider decision-making process of clinicians and patients is more controversial.*

As the use of QALY is useful in some decision-making situations but not useful in others (Kind et al. 2010) the current study uses QALY only at the macro-level of investigation, that is, when it reports the BCA from the perspective of New Zealand society. The micro and meso level BCA do not include QALY in their measurements. This means that the results will be useful in a range of decision-making situations.

MERGING PERSPECTIVES ON VALUE

The current study combines accounting and economic methodologies to measure the value created and captured by two clinical trials. Accounting researchers borrow extensively from the economics literature. Many management accounting techniques used for decision-making are based on the economic theory of marginal analysis. Accounting researchers are therefore interested in the analytical tools and theories of economics (Milne 1991; Bryer 1994; Shiozawa 1999 and Scapens 1991). Similarly, the accounting literature on inflation has relied on the economic theories of income (Milne 1991). Shiozawa (1999) identifies a so far untapped interdisciplinary research potential between accounting and economics and calls for more collaboration between these disciplines.

In practice, the division between accounting and economics and in particular the division between accounting and economics applied within the health sector is not precise. Rapid advances in medical technologies and increasing health demands from an aging population mean rationing health services is becoming increasingly necessary (Scheifele 1997). Economic methodologies can identify the comparative values used in resource allocation while at the same time accounting methodologies can report the results of resource allocation decisions (Wynn-Williams 2011). A good example of this is when PHARMAC uses the economic method of cost utility analysis to assist resource allocation, but applies accounting methodologies for budgeting and the reporting of any savings made (Wynn-Williams 2011). Van Peursem, Pratt and Lawrence (1995) assess economic efficiency by using financial ratios and profit and loss account ratio measures to compare cost inputs with revenue outputs. Other accounting methods include return on investment indicators and profit calculations (see for example, Carpenter 1986, Cleverly and Harvey, 1992 and Beauvais and Wells 2006). This approach, however, presumes a profit motive which is not always present (Van Peursem *et al.* 1995).

Taking a macro view rather than a micro view provides a wider meaning to the accounting terms ‘profitability’ and ‘capital appreciation’ and shows increasing overlap between this discipline and that of economics. As Van Peursem *et al.* (1995 p48) highlight:

> *If health institutions are formed in the interest of net positive productivity, then profit is in effect the net financial contribution made by all public institutions to society. This idea has been incorporated into a number of cost-benefit analyses within the medical*

> *management literature. Costs in this context are usually considered in terms of net costs: net costs comprise the difference between the present value of medical costs now and in the future to treat a patient, less the present value of wages that would have been lost if the patient had forgone treatment.*

The challenge of combining economic and accounting methods is to ensure that users perceive common meaning. (Wynn-Williams 2011). To avoid confusion, this thesis adopts three key definitions. First, a benefit is anything that someone perceives as adding positive value. A cost is anything that someone perceives to add negative value. Outcome is a state or condition of society, the economy, or the environment; and includes a change in that state or condition (Public Finance Act 1989). In other words, outcomes relate to the effects of the addition of adding positive or negative value. Thus, benefits and costs produce outcomes. Costs and benefits are closely linked and may lie across a common continuum – what may be a cost to someone is a benefit to another. Sen (2000 p938) reasons that in BCA, '….*costs are seen as forgone benefits. Thus, benefits and costs are defined, ultimately, in the same space.'*

As discussed earlier, the empirical study reported in this thesis uses BCA to analyse the value of conducting clinical trials in a publicly funded hospital. Accountants use BCA for the following reasons: First, BCA uses accounting information such as costs and charges (Oakes, Considine and Gould 1994). Second, BCA assists the functions of measuring financial performance, allocating resources and controlling expenditure, which governments as funders of health-care look towards accounting to fulfil (Robson 2007, Chua and Preston 1994). Third, naturalistic (in situ) research investigating how accounting numbers are used in real situations can raise important disciplinary insights (Broadbent and Guthrie 2008, Baxter and Chua 2003, Oakes *et al.* 1994). Finally, an analysis of benefits and costs can provide the data needed for evidence-based financial management and provide critical data to support management decisions in health care (Finkler, Henley and Ward 2003). By providing estimates of value that are comparable across treatments and programs, economic evaluation can identify the trade-offs involved in choosing among interventions. To achieve health maximisation, decision makers implement the interventions that generate the highest value. Used in this way, economic evaluation becomes a powerful tool to inform 'complex resource allocation decisions' in the health sector (Gold et al. 1996).

Thus, both accounting and economic methodologies contribute to the current study.

STAKEHOLDER PERSPECTIVES ON VALUE

In the past decade the health sector has increased its engagements with both profit-orientated and non- profit organisations (Broadbent and Guthrie 2008 and Cordery *et al.* 2010). Building positive relationships with stakeholders has therefore become increasingly important. Stakeholder theory is the most prominent in studies of stakeholder relationships (Ayuso, Rodriguez, Ricart 2006 and Barrett and Scott 2008). Stakeholder theory has developed from an interdisciplinary research base, with the view '*to explain and predict how organisations function with respect to stakeholder influences*' (Rowley 1997 p895). A stake is defined as an '*interest', 'claim' or 'share' in an organisation*' (Mallik and Mitra 2006 p10). Freeman defines a stakeholder as '*any group or individual who can affect or is affected by the achievement of a corporation's purpose'* (Freeman 1984 p46). Generally, stakeholder theory advocates that to ensure survival and success in the long-term organisations should consider the impacts of their actions on all stakeholder groups (Collier 2008). Mallik and Mitra (2006) report that stakeholder theory was first recorded in an accounting publication in 1975 (Accounting Standards Steering Committee 1975. The committee suggested that in addition to its responsibilities to shareholders firms are accountable to '*persons or groups having reasonable right to receive information'* (Accounting Standards Steering Committee, 1975 p17).

Stakeholder theory incorporates a range of ideas and approaches. Donaldson and Preston (1995) use three classifications 1) normative, 2) instrumental and 3) descriptive. Normative approaches indicate how organisations should behave in relation to their stakeholders. Instrumental approaches prescribe ways for organisations to relate to their stakeholders to maximise outcomes and descriptive approaches record how organisations actually behave in their relationships with their stakeholders (Jones and Wicks 1999).

Gray *et al.* (1997) raise the importance of consultancy with stakeholder groups. Gray *et al.* 1996) propose a 'polyvocal' citizenship approach to ensure that every stakeholder has a 'voice' in the organisation. This perspective appears to empower stakeholders and enables them to reflect on their experiences, values, interests and concerns (Cotton, Fraser and Hill 2000; Hill, Fraser and Cotton 2001). However, a number of scholars are critical of the suggestion that active stakeholder engagement creates value for all (see for example, Owen et al. 2001; Belal 2002; Dey 2000; Gray 2000, 2001 and Thomson and Bebbington 2004). Thomson and Bebbington,

(2004) argue that organisational interests may bring power that controls the dialogue agenda in stakeholder engagement exercises. Taking this concern into account, O'Dwyer (2005) recommends the structure of stakeholder engagement should be open and allow as much freedom as possible for participants to set the agenda.

Similarly, Lehman (1995, 1999 and 2001) and Ullmann (1985) suggest that accounting is a moral discourse that should maximise the good of the entire community and advocates open and transparent access to information.

Following a review of 125 accounting studies that use stakeholder theory Roberts and Mahoney (2004) identify three approaches to stakeholder analysis; (1) managerial agency, (2) organisational and (3) societal. They find that these research approaches differ in both their methods and their results. The managerial agency approach considers that managing stakeholders' interests will maximise the organisation's performance (Cornell and Shapiro 1987, Hill and Jones 1992 and Mallik and Mitra 2006). The organisational stakeholder approach promotes the building of mutual relationships between management and stakeholders (Bendheim, Waddock and Graves 1998). The key difference between using a managerial agency approach or an organisational approach lies in the view of the nature of the relationship between management and stakeholders (Jensen 2002 and Cornell and Shapiro 1987). An organisational approach views management and stakeholders as having a co-operative relationship. This contrasts with the managerial agency approach, which views the relationship as adversarial (Phillips 2003). Societal approaches investigate the firm from the perspective that the organisation may cause more harm than good for community stakeholders (Roberts and Mahoney 2004). In doing so, they are usually critical of neoclassical economic theory and the laws governing property rights, the role of institutions and the role of the state (Zajac 1995).

Supporters of stakeholder theory consider the organisation's interactions with stakeholders in terms of independent, dyadic relationships (Rowley 1997). Researchers seek to identify how organisations recognise and act upon their various stakeholders claims or alternatively how stakeholders act upon the organisation (Scholl 2001). This view of dyadic, 'hub and spoke' relationships does not acknowledge the collaboration between stakeholders and fails to capture the potential multifaceted interactions within the stakeholder network (Mattingly 2004; Frooman 1999 and Rowley 1997). These authors suggest a more accurate picture of stakeholder

relationships is of a dynamic, complex network of multiple intertwining connections (Neville and Mengue 2006).

Stakeholder theory has its origins in private–sector profit making organisations (Scholl, 2001). Donaldson and Preston (1995) view stakeholder theory as applicable only to the private sector and argue that private firms are governed by different principles from those of public sector organisations and therefore should adopt different approaches. In contrast, Scholl (2001) considers there may be value in applying at least parts of stakeholder theory principles to management decision-making in public-sector organisations. Scholl (2001 p13) reasons;

> *even though most public-sector managers perform their tasks for different ends (e.g., public interest) as opposed to their private-sector counterparts (e.g., survival of the firm, or profit), their decisions have the same capacity of affecting individuals or groups when pursuing their organization's objective.*

Scholl (2001) observes that a recent change within the public sector has meant public management responsibilities more closely resemble private-sector management tasks. Taking a stronger view, the Securities Commission, New Zealand points out that:

> *Stakeholder interests have a particular significance for public sector entities with a public good purpose. These entities operate on public funding, and need to pay careful attention to their public stakeholders.*

The above quotation suggests that a unique relationship exists between public stakeholders and public entities. Collier (2008) applies a stakeholder-agency model and hub and spoke approach to explain the nature of this relationship. He finds the role of the manager is to be accountable to the multiple stakeholders and to prioritise the different claims of those stakeholders. He identifies governance at the centre of contracts between all stakeholders where there are both economic and social concerns (Collier 2008 p937):

> *There is, or at least should be, accountability to each of these stakeholders in terms of the organization's satisfaction of their economic, legal or moral obligations. However, stakeholder salience implies competing interests amongst stakeholders and the need to resolve conflicts. Therefore, an important role for governance is to assess the competing needs of stakeholders, and to balance and/or prioritise those needs.*

Wheeler et al. (2003 p14) raise three questions that organisations might ask of their business activities:

> *1) Is our value proposition feasible? Can it be done within the currently accepted societal framework of how we treat each other? Does it operate at Level 1 (do minimum harm) or at Level 3 (do maximum good)?*
>
> *2) Is there support for the proposition from those groups that are affected? Is there a process for gaining stakeholder cooperation and support for the proposition? Is value created for each stakeholder group in a synergistic way, avoiding excessive trade-offs?*
>
> *3) Can the value that is created be sustained over time — economically, socially and environmentally?*

They argue that projects which fail any of these questions risk failing to create lasting value and eventually will not be sustainable. The current study does not ask these questions directly. The multiple stakeholder perceptions strand of the current study asks informants to identify the costs and benefits for each identified stakeholder group. This provides sufficient information to answer the first two questions asked by Wheeler *et al.* (2003). The economic outcomes strand quantifies the costs and benefits of clinical trials. This provides valuable data to contribute to the answer to question three.

The literature reveals a number of proposals for identifying, classifying or mapping stakeholders according to attributes such as power, influence and interest (see for example, Mitchell *et al.* 1997). Clarkson (1995) argues that a stakeholder has some form of capital (either financial or human) at risk and, therefore, has something to lose or gain depending on an organisation's behaviour. Kochan and Rubenstein (2000 p373), suggest three criteria for identifying significant stakeholders:

> *1 They supply resources that are critical to the success of the enterprise.*
>
> *2. They place something of value "at risk"; that is, their own welfare is directly 'affected by the fate of the enterprise.'*
>
> *3. They have 'sufficient power' to affect the performance of the enterprise, either favourably or unfavourably*.

Since stakeholder theory emphasises values such as participation, inclusion and mutual dependence (Wheeler *et al.* 2003) it provides an appropriate theoretical framework to evaluate the value created by the stakeholder relationships in the empirical study described in the next chapter.

Stakeholder theory provides justification for the choice of stakeholders in the current study. Collier (2008) identifies the stakeholders in this quasi government sector as consisting of government, lenders, service recipients, suppliers, employees and taxpayers. The current study uses this as a base but adopts minor changes to accommodate the unique environment of sponsored clinical trials. The final list of stakeholders for the current study is trial participants; trial participants' family member and caregivers; CMDHB staff; researchers; the Counties Manukau community; government, government bodies and politicians; and members of the pharmaceutical industry. The current study does not adopt a specific approach to stakeholder analysis. Instead, it asks open questions to all stakeholder groups that allow stakeholders to adopt the approach that best fits their worldview. Chapter 4 will provide further rationalisation for this selection.

Stakeholder theory and legitimacy theory have grown from the broader political economy perspective (Gray et al, 1996; Deegan 2002). While there are differences between stakeholder and legitimacy theory, they both focus attention on the relationship between the organisation and its operating environment (Neu, Warsame and Pedwell 1998). The main trust of legitimacy theory is for organisations to validate their activities (Tilling 2004). Mathews (1993 p350) offer a good explanation of legitimacy theory;

> *Organisations seek to establish congruence between the social values associated with or implied by their activities and the norms of acceptable behaviour in the larger social system in which they are a part. In so far as these two value systems are congruent, we can speak of organisational legitimacy. When an actual or potential disparity exists between the two value systems there will exist a threat to organisational legitimacy.*

Organisations can safeguard or restore their legitimacy by including, informing and educating their stakeholders, with the view to changing their perceptions, averting their focus to other matters, or changing their expectations (Parker 2005, Hybels 1995). There is evidence of increasing lack of public trust in the large pharmaceutical companies and in the clinical trials; they conduct (Bushfield 2006). This loss of trust has become a serious concern to the industry (Angell 2008, Torralba, Quimorio and Kahn 2009) and is resulting in reduced recruitment rates and increased costs of clinical trials (Scharke 2008). Trust incorporates both interpersonal

relations and institutional systems (Carter 2009). Bok (1978) identifies a relationship between trust, honesty and consistency and considers three different kinds of trust (1) that you will treat me fairly, (2) that you will have my interests at heart and (3) that you will do me no harm. Trust is also a future orientated coping technique, where, in situations in which individuals perceive the possibilities of the future as complex and uncertain, they seek to reduce the complexity through the act of trust (Luhmann 1979). Further, Luhmann suggests the individual will determine if the trustee is worthy of trust in the management of future events based on the information available in the present. Therefore, to build future trust clinical trial professionals must ensure participants perceive their actions as trustworthy. Getz (2008a p18) identifies a growing distrust:

> *Although the public clearly holds positive attitudes about the general importance of clinical research, the same cannot be said for public trust in the professionals who oversee, manage, and support that research. Distrust in clinical research professionals, and in those organisations responsible for ensuring patient safety, has increased dramatically.*

These issues manifest most strongly in North America, which has a different legislative framework applying to pharmaceuticals industry activities from that in New Zealand. The strict legislative framework in New Zealand may have the effect of limiting similar criticism of the pharmaceutical industry and the clinical trials they sponsor. Pharmaceutical companies may try to legitimise their organisation by highlighting the societal benefits of the clinical trials they sponsor. The current study allows stakeholders to identify any trust issues they may have with pharmaceutical companies when they identify their perceptions of the costs and benefits of clinical trials.

CONCLUSION

The review of the literature in this chapter provides an insight into the concept of value and sets the theoretical foundations for the empirical study presented in the chapters that follow. The chapter first reviews the published literature on value and its measurement. There is no one common understanding of value however the accounting, economic and health disciplines offer useful insights into its nature. The chapter then considers the literature on value in healthcare.

Around the world, all health systems are struggling with rising patient demand and limited resources that create a new urgency for better value healthcare. Porter (2010) produces a model for measuring value in the health sector. This model will be adapted to form the basis of measurement in the current study. Accounting has a major role in cost measurement in the health sector. This chapter explores the historic significance of its involvement. Accounting researchers in the health sector borrow extensively from economic literature. The chapter explores economic methods for measuring value in health care and justifies the choice of BCA for the current study. The chapter completes a review of the literature on stakeholder perspectives before exploring the normative foundations of economic evaluation.

The purpose for initiation of this review was context specific. The initial focus on identifying the nature of value influences both the selection of literary material and the development of the empirical study described in the following chapters. The next chapter, chapter 3, continues the literature review by reporting the contribution from empirical studies that focus on the benefits and costs of clinical trials. Chapter 4 identifies the methods the study adopts. Chapter 5 presents the results from the economic strand of the study. Chapter 6 presents the results from the multiple stakeholder perceptions strand of the study. Chapter 7 concludes the thesis.

3. REVIEW OF THE EMPIRICAL RESEARCH

This chapter reviews the literature reporting empirical studies that focus on the benefits and costs of clinical trials. The chapter classifies the studies into eight sections that correspond to the questions asked of stakeholders in the multiple stakeholder perceptions strand of the current study. These groups are: (1) trial participants (2) the family, community and other caregivers, (3) staff, (4) members of the pharmaceutical industry, (5) DHBs (6) the New Zealand community, and finally (7) the international community. The empirical study's provide insight into past approaches to the measurement of the benefits and costs of clinical trials and informs the approach to the current study. The chapter then presents a number of key theoretical models, which demonstrate how the costs and benefits of clinical trials may be classified.

THE BENEFITS AND COSTS FOR TRIAL PARTICIPANTS

There is limited research on the benefits and costs associated with clinical trial participation; however, some evidence suggests that patients have better clinical outcomes when they enrol in a clinical trial than those from standard care. Miles, Bingham and Dilts (2002) argue that enrolling patients in a clinical trial is one of the most effective methods to improve patient outcomes. They cite several studies to support their views. Simone and Lyons (1998) examine health records for a 30-year period and discover that over this time 90 percent of American children with leukaemia were enrolled in clinical trials. They report that five-year cure rates for leukaemia sufferers over the same period moved from 0 percent to nearly 80 percent.

From the perspective of the trial participant, the procedures during a clinical trial may not be that different from that of standard clinical care. In a trial a medical history and examination are performed, a decision is made on whether a person is a candidate for a trial, followed by the participant being given the new medicine and monitored, often as an outpatient while the new agent is evaluated (Johnston 2007). Johnston notes two key differences between a trial and standard treatment: the number of forms to fill out and the additional tests required. These activities can take considerable time. He suggests that improving the integration between clinical trials and standard care may lead to significant savings in the costs of clinical trials. Lee (1999) takes a different view and identifies a significant difference between patients and trial

participants. He argues that in clinical research an individual patient's needs may become secondary to the conduct of the trial protocol. She argues that this may occur even if researchers design clinical trials with the participant's needs in mind. Lee believes that there will always be inherent conflict in clinical trials between a physician-scientist's dedication to the promotion of health for the individual patient and loyalty to the outcome of clinical research.

Watson (2006) itemises considerable benefits for trial participants. He asserts that PHARMAC control has reduced the availability of advanced pharmaceutics for New Zealanders compared to other countries (for example Australia) with the result that many patients can only access innovative treatment if they purchase it themselves or enrol in a clinical trial. Watson also considers that because of the rigorous attention to detail and extensive review process involved in the trial protocol, patients involved in clinical trials have better outcomes than patients undergoing standard treatments do. There is concern however over the public's perceived lack of confidence in pharmaceutical companies (Silversides 2009). Silverside suggests that perceptions of pharmaceutical companies by the public have changed from 'discoverers of new medications' to one of 'commodity providers' which has led to difficulties recruiting patients for trials with the exception of trials for cancer drugs (Silversides 2009 p22). Participation in a clinical trial can also create additional demands on volunteers. Before a volunteer can join a trial, they must complete lengthy consent forms (Malakoff 2008). Then some research protocols 'require volunteers to undertake numerous time-consuming and sometimes painful medical procedures' (Malakoff 2008 p210). The number of procedures undertaken in trials also appears to be growing, by 1999 the typical study involved ninety-six total procedures, while by 2005, the average number of procedures have grown by more than fifty percent to 158 (Getz 2008a).

The literature identifies several studies that investigate patient involvement in trial design (Hanley, Truesdale, King, Elboure and Chalmers 2001) informed consent (Lantos 1993) the motives for participation in clinical trials (Lee and Breaux 1983) and attitudes toward participation (Schuber 2008). The motives and perspectives of those who agree to enrol in clinical trials provide insight into perceived benefits from participating in clinical trials. The majority of patients who are asked to participate in clinical trials agree to do so (Lee and Breaux 1983) and some refer to it as 'a fascinating and stimulating experience' (Burnet, Earl, Charge, Cox, Benson, and Purushotham 2004 p34). Participants report personal satisfaction and a sense of purpose when participating in clinical trials even when there is no clinical benefit to the

patient (Cox 1999). Other psychological benefits include the impression of being cared for by experts, an enhanced sense of hope and altruistic feelings (Burnet et al. 2004). Understanding why people refuse to enrol in a clinical trial provides a perspective on the perceived costs of participating in trials. Patients decide not to participate in a clinical trial for a variety of reasons. Ellis observes that '*public understanding of clinical trials has a strong connotation of medical experimentation and subjects being used as guinea pigs*' (Ellis 2000 p939).

TABLE 3-1 FACTORS THAT MAY HAVE A NEGATIVE INFLUENCE ON PARTICIPATION IN CLINICAL TRIALS (ADAPTED FROM ELLIS 2000 P940)

Doctor factors	Logistic difficulties	Unaware of trial Lack of time Lack of resources for example data management Financial constraints Type of practice (public versus private) Difficulty with ethics requirements Identification of eligible patients
	Personal difficulties	Effect on doctor-patient relationship Discomfort with randomisation Difficulty with informed consent procedures Preference for a particular treatment Overall too difficult (too much time and effort) Lack of acknowledgement Referring doctors opinion of trial value
Patient factors		Demographics for example age, education, income Faith or trust in doctor Preference for a particular treatment Concerns about treatment toxicity Dislike of randomisation, experimentation Loss of control Practical issues such as inconvenience Access to free medical care
Trial factors		Poorly designed or complex protocols Presence of a no treatment arm Large difference in treatment arms for example surgery versus radiotherapy Toxic therapy being tested Standard therapy arm not considered standard therapy Eligibility requirements too narrow Irrelevant or unimportant trial questions

Featherstone and Donovan (1998) consider the uncertainty associated with the randomised allocation of treatment as a reason why people decide not to participate in trials. Patients may refuse to participate in trials because they are unwilling to hand-over their clinical decision making to a researcher (Ellis 2000). Some people express concerns that participating in a clinical trial will inhibit their return to normal life following illness while other cost factors they consider are demands on personal time and the stress of finding car parking (Burnet et al. 2004).

Ellis (2000) summarises the factors influencing participation in clinical trials into three areas: doctor factors, patient factors and trial factors (Table 3.1). The United States General Accounting Office (1999) investigates the factors affecting patient participation in trials. They find that patient's decisions whether or not to participate is influenced by the type of disease the patient has the type of trial, phase of the trial and other specific circumstances. They also find participant concerns over logistics an important influencing factor in trial participation. The practical concerns of participants are magnified because clinical trials are less flexible and place greater requirements on patients. The United States General Accounting Office (1999 p13) concludes:

> *Requirements can be time consuming and impose financial and childcare burdens on individuals who may be seriously ill. Moreover, such demands can add to stress by separating patients from family support and making it difficult to meet work obligations.*

Henzlova, Blackburn, Bradley and Rogers (1994) question 3522 participants enrolled in a long-term trial. Their questions focus on the primary reason for enrolment, positive and negative experiences, and changes in routine behaviour. Their survey results show the most common reasons for enrolment are the endorsement by the primary physician, a desire to contribute to medical science and wanting to help others. Although the majority of the informants are satisfied with their trial outcome and are happy to participate in a future clinical trial, they express some negative experiences including difficulties with transportation to and from the clinic and the numerous staff changes. Surprisingly several participants report changes in their smoking habits, alcohol intake, and diet, despite the absence of behavioural interventions in the study protocol. This may be due to participants seeing enrolment in the trial as a positive action, which precipitates other positive changes.

Cultural differences may also affect the participant's perception of clinical trials. Hussain-Gambles (2004) uses semi-structured interviews to study South Asian patients' views and experiences of participating in clinical trials in England. While most aspects of the trial

experience are similar to 'white' informants, Hussain-Gambles considers being aware of South Asian under-representation (especially in clinical trials that explore illnesses prevalent in their community) is a strong motivational factor. Barriers to trial participation, which they identify, include language problems, female modesty and preference for female trial staff. Paz (2005) also identifies cultural barriers to participation, particularly from cultures in which the family plays a pivotal role in healthcare decisions may minimise the individual's choice. Paz (2005) suggests that culture may also have a positive effect on trial participation especially by those cultures that value community responsibility over individuality. Paz asserts the researcher's sex or race may influence the researcher's ability to obtain informed consent may unintentionally influence the feeling of trust perceived by the potential participant. This is an aspect worth exploring further in the New Zealand context particularly because of the underrepresentation of Maori in clinical trials.

Researchers use both quantitative and qualitative methods to gain an understanding of trial participation and its impact on participants (Donovan, Brindle and Mills 2002). In-depth interviews are one of the most effective ways to understand the psychological, emotional and social impact of taking part in a clinical trial from the perspective of the patient (Cox 2003). Participants involved in phase I and II oncology trials describe a dynamic and changing experience that has a different impact and meaning as they progress through the trial process (Cox 2002). Several studies report behaviour changes in participants involved in a clinical trial. Participation in a clinical trial can have a positive effect on glucose control independent of any therapeutic intervention in participants with diabetes (Gale, Beattie, Hu, Koivisto and Tan 2007, McGuinness 2007, Worth, Home, Johnston, Anderson, Ashworth, Burrin, Appleton, Binder and Alberti 1982, DeVries, Snoek, Kostense and Heine 2003). Worth et al. (1982) observe initial improvement in diabetes control followed by deteriation that they suggest is due to declining enthusiasm. There may however be a potential lasting impact. DeVries et. al.(2003 p360) note:

> *In itself the experience of having been able, be it temporarily, to actually enhance glycaemic outcomes while preserving emotional well-being shows 'it can be done' and reinforces a more positive attitude and the patients feelings of diabetes self-efficacy.*

A Quintiles study ranking staking groups on how much value they add to healthcare concluded that '*patients themselves are not doing enough to improve their own health outcomes'*(Quintiles 2011 p9).The current study investigates two clinical trials focusing on the cardiovascular

complications of diabetes. With the increasing prevalence of diabetes in the Counties Manukau region (CMDHB 2009b), improving patient self-control is an important objective.

Children and young people gain education leading to improved self-management of their illness from trial participation (McGuinness 2007). One explanation of this behaviour change is that better access to staff provides opportunities for participants to discuss and gain a better understanding of how to manage their illness. In addition, working on a clinical trial may encourage health care workers to respond more eagerly to their patients (Majundar et al. 2003).

The literature paints a general positive picture for participants of trials. Little mention is made of the possible risks or side effects. The most prominent cost appears to be the time taken to attend trial sessions and the undergoing of considerable testing. Having reviewed the published literature on the benefits and costs to the trial participant, the researcher will now consider the literature from the perspective of the family and community based caregivers.

THE BENEFITS AND COSTS FOR FAMILY AND CARE GIVERS

Researchers seldom investigate the views of family members and caregivers. Williams *et al.*, (2006) consider families members perceptions of clinical trials and suggest family members are generally supportive when trial participants consent to joining a clinical trial. Hanson, Magnusson Nolan and Nolan (2006 p326) call for patients and caregivers

> *to be more actively involved in research, not simply as subjects, but in helping to identify important questions, in shaping methodology and also in data collection, analysis and the dissemination of results*

White (2004) uses multi-professional focus groups, patient and relative interviews and questionnaires to canvas trial perceptions from 101 palliative care patients and 100 relatives. She finds strong support for trials from both patients and their relatives. The trial design and the possibility of side effects are very important factors in both the patients and their relative's assessment of the clinical trials. White suggests that clinical trials are more likely to be successful if researchers consider the views of patients and their relatives during trial development.

There are also benefits for community support groups to having pharmaceutical companies conducting trials in their districts. Watson (2006) maintains that community groups including

research and public health related organisations benefit from the generous donations given to them by pharmaceutical companies. New Zealand examples include GlaxoSmithKline's sponsorship of Youthline and Pharmacia's sponsorship of the Arthritis Foundation. A report by O'Connell and Mosconi (2006) views community support groups as important allies in the drug development process. They suggest that community groups provide important information to potential participants either directly or by alerting their members to other sources of information such as the websites of research consortiums. This is particularly important, as the public's expectations regarding the benefits of clinical trials are higher than physicians' expectations (Cassileth, Lusk, Millerand Hurwitz 1982). In addition, O'Connell, and Mosconi observe that patient support groups are a key to building trust between researchers and potential participants. Patient support groups are able to provide independent advice and support to participants and are often able to lobby for funding for more research into the area of their concern. The review next considers the benefits and costs of sponsored clinical trials from the perspective of the staff involved.

THE BENEFITS AND COSTS FOR STAFF

The staff employed to conduct a trial are crucial to the trials success. Doctors and referring agents have a strong influence over whether a person will agree to participate in a clinical trial. Taylor and Kelner (1987) conduct a survey of oncologists to identify attitudes and practices towards clinical trial. They find '*the necessity of obtaining informed consent reduces the willingness of oncologists to participate in clinical trials intrudes into the doctor patient relationship and has a negative impact on patient care*' (Taylor et al. 1987 p135). The survey also reveals oncologists concern that enrolling patients on clinical trials leads to: '*less effective communication and flexibility in disclosure; decreased patient confidence in the oncologist, leading to decreased patient compliance; and conflict of interest between the oncologist's roles as care-giver and scientific investigator*' (Taylor et al. 1987 p35). Helman (1979) also suggests, when a doctor takes on a role as a clinical investigator, this can conflict with the doctor patient relationship. Other studies find that doctors may have difficulty discussing with their patients the option of clinical trials and the uncertainty that trials pose (Fallowfield 1995). There are also ethical difficulties associated with seeking informed consent directly after diagnosing a patient

with a serious or life threatening illness (Baum 1990). This results in doctors being unwilling to enrol their patients in clinical trials.

A 2007 study by Sale, asks nurses and radiation therapists in a cancer centre about their experiences with clinical trials. They identify some ethical concerns including the ability of trial participants to jump waiting lists for scheduled procedures and the use of placebos. They report treating participants of clinical trials can add to the workload of radiation therapists especially when adhering to complex research protocols. Often staff do not have time to fully familiarise themselves with the protocol which makes adhering to it difficult. Sale finds some nurses and radiation therapists experience a lack of meaningful involvement in clinical trials. They feel other staff undervalue their work. They require greater involvement in the decision-making within the clinical trials process. However, both nurses and radiation therapists are supportive of clinical trials feeling that the benefits to participants are greater than the disruption for themselves. They believe participants benefit by obtaining better treatment and by more quality contact time with staff, which allows them to be better informed.

The difference in values between working as a clinical nurse and working as a research nurse has been widely discussed (Davis, Hull, Grady Wilfond and Henderson 2002). Sequin (1990) views the experiences as very similar with both roles requiring the assessment of needs, the development and implementation of plans and the collection of data. Hicks (1996), however holds an opposing view believing that to undertake research requires the relinquishing of the essential characteristics of nursing stating (p358):

> *Research, irrespective of the methodology adopted, calls for an entirely different set of core values from those demanded of nursing, requiring detachment rather than caring concern, objectivity rather than subjectivity, hard-nosed analysis rather than intuition, pro-activity rather than reactivity.*

Davis et al. (2002 p241) identify three often-conflicting advocacy roles which researchers must balance (1) patient advocacy (2) subject advocacy and (3) study advocacy. Patient advocacy requires the researcher to have the patient as their primary task. Metaphors such as mothering describe the patient advocacy role. Subject advocacy requires a commitment to the rights and welfare of the individual as a research subject. The metaphor 'lawyer' to describes subject advocacy. Finally, study advocacy requires a commitment to advancing research objectives and gathering quality data. Acting for the 'protocol police-force' describes study advocacy. Table

3.2 compares these advocacy roles. Meeting all of these roles can be ethically challenging (Grady and Edgerly 2009).

TABLE 3-2 ADVOCACY ROLES (SOURCE: ADAPTED FROM DAVIS ET AL. 2002 P415).

	Patient Advocacy	Subject Advocacy	Study Advocacy
Primary Commitment	Patient's welfare	Rights and welfare of the individual as research subject	Advancing research goals, gathering valid, clean data, via good recruitment and retention of subjects
Duration of relationship with patient turned subject	Before, during and/ or after	Before and during	Study specific
Metaphors	'mothering', 'taking care of'	'lawyer'	'policeman of protocol', 'teacher'.

Successful trial outcomes are dependent on dedicated research staff. There is little documentation on the experience of staff and researchers in New Zealand. Watson (2006) believes conducting commercially sponsored trials can be better than trying to attract government funding (Watson 2006 p26):

> *There is inadequate funding to retain and attract leading professors and researchers who otherwise struggle on government health funding. Indeed, a significant amount of researchers' time in this country is spent trying to write grant applications for the relatively small pool of research funding*.

Factors that influence the participation of physicians in clinical trials can provide a window to the perceived benefits by this stakeholder group. In one study of this type, Dev, Kauf, Zeky, Patel, Heller, Schulman and McHutchison (2008) investigate factors influencing the participation of physicians in clinical research in the USA. They survey 1050 gastroenterologists and haematologists and identify a preference by physicians for industry-sponsored research, low complex trial protocols and studies of short duration. Finding that the greatest barrier to participation in clinical research is a lack of adequate resources leads to the recommendation that larger hospitals establish centralised research support services. Other identified barriers include excessive trial costs not covered by the trial sponsor, perceived inferior trial medication(s) compared to standard therapy and ethical concerns.

Clinicians and hospital staff may also benefit from being involved in clinical research including the opportunity to obtain experience with otherwise unavailable new treatments and technology, the development of networks with clinicians of similar interest around the world and participation in education and training programmes (Watson 2006). Several medical education programs in New Zealand receive support from pharmaceutical companies and pharmaceutical company sponsor training in key areas of clinical trial management and regulatory compliance. New Zealand researchers may also be able to add local research questions to those of the multinational pharmaceutical trials, enabling the researcher to undertake local research while developing international recognition (Watson 2006).

The opportunity to engage in clinical research may assist staff retention. In one New Zealand study, Daniels (2004) finds that a major impact on nurses' intention to leave their position is the motivation to develop additional skills and promote health care changes. (Daniels 2004 p127):

> *Both research and media reports of nurses' experiences of high workloads, stress, burnout and poor patient outcomes have been associated with intent to leave the job. However, intent to leave the job in nurse participants in this study was not directly motivated by high workloads or burnout but was motivated by the need to develop further skills and knowledge that could be used to create positive change in the health environment.*

Providing opportunities to develop skills and effect change through clinical research may therefore encourage retention.

Doctors who are researchers in a trial do not always prescribe the new medication after they complete the trial. Majumdar, Chang and Armstrong (2002), find that doctors on sites that have taken part in a trial for Angiotensin-converting enzyme (ACE) inhibitors are no more likely to adopt ACE inhibitors for patients with myocardial infarction than are doctors from sites that have not taken part. Meineche-Schmidt, Hvenegaard and Juhl (2006) find conflicting evidence surrounding the long-term effects on doctors following trial engagement. They find that doctors continue to use treatments from the clinical trial after the trial has ended and prescribe trial medications more often than non-trial doctors prescribe them.

Some writers express concerns about the time demands of research engagement. Getz (2007a) argues that compliance requirements place unreasonable demands on study staff time and focus and therefore threatens study conduct performance. Site feasibility assessments are one area that

needs improvement writes Getz (2008c). Site feasibility studies require resources from both sites and the sponsor yet, Getz argues, sites often do not have sufficient information about the proposed study to provide accurate projections, thus the completed feasibility study becomes a meaningless paper exercise.

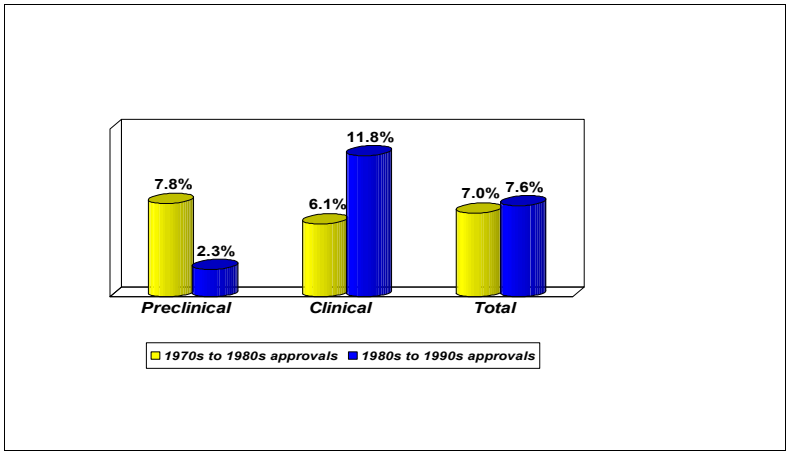
The benefits of clinical trials as perceived by trial participants and medical staff may be influenced by both the culture and the healthcare system in operation in the trial host country in which the trial. In one Japanese study, Ono et al. (2000) identify a lack of cost consciousness and an indifference to treatment costs in both patients and practitioners, which they attribute to the Japanese universal health insurance system. This indifference to costs they claim impacts on the conduct of and potential financial benefits of clinical trials. It is not known how culture influences the cost of running a trial in New Zealand.

THE BENEFITS AND COSTS FOR PHARMACEUTICAL COMPANIES

Clinical trials are the final stage in the development of new pharmaceutical products. In commissioning a clinical trial, the sponsoring pharmaceutical companies face high financial risk involving considerable resources (Murphy and Topel 1998). This section reviews the literature on the benefits and costs of sponsored clinical trials from the perspective of the pharmaceutical company.

The cost of conducting clinical trials is increasing rapidly (Johnston 2007; DiMasi 2008; Collier 2009a). DiMasi et al. (2003 and 2004) show the cost of clinical trials increase five times faster than preclinical costs between the 1980s and the 1990s (see figure 3.1). The literature provides a range of explanations for this trend. Johnston (2007) ties trial costs to health-care delivery, which also has rising costs. (Collier 2009a, Getz 2008a and Kaitin 2006)blame the increased numbers of trials undertaken, larger participant numbers and increased enrolment criteria mean higher recruitment costs) DiMasi (2008) identifies longer, more complex clinical trials with more procedures per patient (Christie, Gabriel and Dear 2007) ethics and other regulatory requirements .

FIGURE 3-1 ANNUAL GROWTH RATES FOR OUT-OF-POCKET RESEARCH AND DEVELOPMENT COSTS (SOURCE: DIMASI ET AL. 2003 P153).



Adding to developer difficulties of participant recruitment is the number of trials they now undertake. Kaitin (2006) reports that figures taken from the top ten pharmaceutical companies show that the number of new drugs the clinical trial stage of development increased fifty-two percent between 2003 and 2005. Recent years have seen the development of longer, more complex and more expensive clinical trials with more procedures per patient (DiMasi 2008). Malakoff (2008) blames this increase in procedures on poor design. He also suggests that having to prove regulatory compliance leads to the ordering of additional procedures. A 2005 study by Kaitin shows that average clinical trial phase time increased twenty-one percent from a low of 5.8 years in 1999 to 2001 to a high of seven years in 2002 to 2004. Collier (2009b) suggests this is due to an increase in the development of treatments associated with chronic and degenerative diseases, which require longer trials that are more complex.

The increase in trial complexity adds to the cost of participant recruitment as well as increasing labour requirements at the trial centre (Johnston 2007). Kaitin (2008) reports an increase in the 1999 to 2005 annual growth rates for protocol procedures including the number of unique procedures and the total procedures of up to 11 percent depending on the trial phase (Table 3.3). Kaitin defines total procedures as 'the number of unique procedures multiplied by their frequency during the duration of the study' (Kaitin 2008 p1). Clinical trials often require testing beyond that needed by researchers to determine efficacy and safety (Johnston 2007). Johnston suggests that the large simple trials researchers perform in Europe are yielding hugely beneficial results and changing neurological practice, yet they have cost a fraction of many American trials.

However, observers predict protocol design complexity will continue to grow as clinical trials demands for diverse, globally based participants increase (Tufts Centre for the Study of Drug Development 2007). New technologies have allowed researchers more information on trial outcomes but in order to capture these advantages more steps have needed to be added to the trial protocol, which has increased costs (Getz 2008a). Regulatory requirements such as site monitoring, comprehensive adverse event reporting and local Institutional Review Board (IRB) negotiations have also contributed to escalating costs (Johnston 2007) with researchers 'ordering up needless procedures in order to be ready for questions from regulators' (Malakoff 2008 p212). Kitson (2002) shows that cutting development and regulatory review times by twenty-five percent would reduce overall drug development costs by US$129 million. Malakoff (2008) feels that developing efficiencies in the organisation of paper work including automation and standardisation will reduce compliance costs. He suggests establishing an accreditation process to recognise excellent research sites and personnel.

TABLE 3-3 GROWTH RATE IN MEDIUM NUMBER OF PROCEDURES PER PROTOCOL 1999-2005 (SOURCE: KAITIN 2008 P1).

		Median Number (2005)	**1999-2005 Annual Growth Rate**
Phase I	Unique Procedures	40	6.1%
	Total Procedures	217	9.5%
Phase II	Unique Procedures	35	5.8%
	Total Procedures	195	12.1%
Phase III	Unique Procedures	33	5.5%
	Total Procedures	132	6.1%
Phase IV	Unique Procedures	32	9.1%
	Total Procedures	99	11.0%

To help stem the rising costs of clinical trials Zycher et al. (2008) promote technological advances in drug-discovery methods, improved preclinical identification of promising compounds, clinical trial designs that produce better information, faster development of the most promising drugs, earlier termination of research and trials of drugs that are unlikely to succeed,

and regulatory adjustments. Meanwhile Collier (2009a) suggests reducing product failures at the later stages of the clinical trial process and improving the participant recruitment process. Getz (2008b) maintains that drug developers should be focusing on between phase efficiencies as a way to reduce costs.

Government policy and regulation of medicines has limited the number of sponsored trials in New Zealand. Pharmaceutical companies sponsoring trials in New Zealand also face the possibility of long-term liabilities as Watson (2006 p14) explains:

> *Once the patient has completed the clinical trial and still requires the medicine used in the clinical trial, the companies allow the patient to continue on the medicine free of charge, until reimbursement. As the possibility of reimbursement for a particular medicine is so low in New Zealand, companies face the very real liability that once a clinical trial has ended, they are morally obligated to provide the medicine free of charge for an indefinite period of time at their own cost. Such a liability is yet another disincentive for companies to perform clinical trials in New Zealand*.

The benefits of clinical trials for pharmaceutical companies include the economic return once the new drug reaches the market. Debates on pharmaceutical pricing often turn to whether higher drug prices support greater company-financed research and development spending. Although there are no published links between the profits from drug sales and the amount spent on clinical trials, there are published links with the amount spent on the broader field of research and development (Comanora and Schweitzer 2007). Giaccotto, Sonterre, and Vernon (2005) argue that after holding constant other determinants of research and development a ten percent increase in the growth of real drug prices results in nearly a six percent increase in research and development intensity. This section has identified a range of benefits and costs to members of the pharmaceutical industry in sponsoring clinical trials. It is not known if New Zealand based stakeholders will have the same perceptions of the costs and benefits as their overseas counterparts. The next section reviews the literature on the benefits and costs to the DHBs who provide the facilities needed for the trials.

THE BENEFITS AND COSTS FOR DHBS

Most sponsored clinical trials conducted in New Zealand take place within public institutions operated by local DHBs although private research organisations perform some sponsored trials (Watson 2006). Conducting clinical trials may provide a range of benefits for the DHB concerned. Watson suggests DHBs could attract clinical trials relating to diseases at which they want to focus as priorities for their region and maintains that significant medical cost avoidance by DHBs can be achieved especially in trial areas such as oncology, which New Zealand has research expertise. He claims that patients involved in trials will have access to the latest medicines at no cost to the hospital (or patient) in terms of treatment costs (radiology, clinical input, overhead expenses) and significantly reduced and in some cases no pharmaceutical cost. Watson stresses that savings to DHBs also occur because of clinical research centres removing patients out of the public system for the duration of the trial.

DHBs can also save by having private clinical research centres in their catchment area, as this will remove patient costs from the public system (Watson 2006). Additional benefits Watson claims are obtainable by maximising infrastructure usage and therefore achieving economies of scale. This means that focusing clinical research in one unit where the use of facilities can be maximised will achieve cost avoidance. Watson indicates potential cost avoidance of tens of millions of dollars to DHBs if clinical trials are increased. He suggests DHBs are not aware of the savings that they can make (Watson 2006 p25):

> *The cost savings to a public hospital generated by enrolling patients in clinical trials should be a significant driver of increased demand by the hospital managers for clinical trials- something that seems to have not been registered on the financial radar of nearly all New Zealand hospitals.*

International studies produce a variety of results on the benefits and costs of clinical trials. The studies noted next, all based on quantitative data, calculate the savings from drug cost avoidance for hospitals running clinical trials. LaFleur et al. (2004) review the study protocols and dispensing data for clinical trials in one unit over two years and calculate the revenue generated and drug cost avoided. They find that drug trial participation achieves substantial drug cost avoidance. In a comparable United States study McDonagh et al. (2000) examine the costs and savings resulting from drug cost avoidance for two organisations during the fiscal year 1996 to

1997. They use pharmacy-dispensing records to tabulate the number of drugs provided free for each study. Drug cost avoidance results in significant savings equivalent to eight percent of the institutions' annual drug budget. Acquired immune deficiency syndrome (AIDS) and oncology trials deliver the highest drug cost avoidance savings. Braunholtz et al. (2001) focus on the immediate benefit resulting from clinical trials. They summarise trial data to determine whether a trial is beneficial or detrimental to patients participating in it. Their findings suggest that trials on average and if conducted well tend to benefit the participants and do not in most instances result in harm. These studies suggest that the conduct of clinical trials offers potential benefits to trial participants and cost savings to the New Zealand health sector.

Clinical trials provide the evidence needed to establish complete medical practice guidelines but it remains unclear whether patients enrolled in trials are similar to those treated in routine practice. It is also unclear whether trial enrolment influences in-hospital treatments and outcomes. One common research design is to compare outcomes on a hospital-wide basis. Kandzari, Roe, Chen, Lytle, Pollack, Harrington, Ohman, Gibler and Peterson (2005) find that patients participating in clinical trials are more likely to receive beneficial therapies and interventions throughout their hospitalisation than non-trial participants are. However, possible preferential recruitment of participants with lower-risk symptoms may have contributed to the observed differences. Using a large sample of 174 062 patients treated at 494 hospitals, Majundar, Roe, Peterson, Chen, Gibler and Armstrong (2008) conduct a quantitative comparative study between hospitals conducting clinical trials on patients with acute coronary syndrome with non-clinical trial hospitals. Although on average the clinical trial hospitals enrol less than three percent of their acute coronary syndrome patients into trials the improvements to patient care and mortality rates are significant and evident across both participating and nonparticipation patients. In addition, they find that increasing the number of patient enrolments in the clinical trials lowers the mortality rates recorded. However, this result may be due to the possibility that hospitals that have a lower mortality rate may be more inclined to participate in clinical trials.

When a pharmaceutical company sponsors a clinical trial, it provides the trial medications and pays a fee for the tests, protocol related treatments and the administration of the trial. The fee includes a surplus, which the research unit is able to invest in its own research projects. Studies using a micro–level perspective investigate the immediate revenue and / or costs of clinical trials.

In one such analysis Emanuel, Schnipper, Kamin, Levinson and Lichter (2003) investigate the non-treatment time and costs associated with clinical trials. They conduct a mock phase III clinical trial involving twenty patients and a twelve-month trial period to estimate the time and costs of thirteen trial activities. The researchers suggest that payments made by the pharmaceutical industry '*off-set and cross-subsidise*' the low payments made by research grants from the not-for-profit sector but warn that these profits may not be large (Emanuel et al. 2003 p4149):

> *Even enrolling subjects onto pharmaceutical company-sponsored trials, in which payments probably exceed costs, could result in substantial profits for physicians only if the condition being studied is so common that a practice or medical centre could enrol many patients who fulfil the eligibility requirements, and only if the trial is relatively short, simple, and with few substantial risks, so that the effort necessary to conduct the trial is modest.*

Most studies that take a meso level perspective of the benefits and costs of clinical trials involve one of two research methods, either (1) they examine the costs of participating in clinical trials compared to patients undergoing standard treatments (for example Fireman, Fehrenbacher, Gruskin and Ray 2000 Bennett, Adams, Knox, Kelahan, Silver and Bailes 2001) or (2) they investigate the benefits from drug and other cost avoidance for hospitals running clinical trials (for example LaFleur, Tyler and Sharma 2004; Perrín and López 2008; and McDonagh, Miller and Naden 2000). Most of these studies compare the costs of treating patients participating in clinical trials with the cost of treating patients undergoing standard treatments. These studies often involve retrospective case controls, use existing databases to allocate costs and are oncology trials. Goldman et al. (2001 p105) however warn of the dangers of generalising from these studies because of the '*unique practice settings, insufficient sample sizes, and the exclusion of potentially significant costs*'.

In a large study into the direct costs of medical care for participants enrolled in twenty-two cancer trials Fireman, *et al.* (2000) investigate 135 case matched participants over a one year period. They review patient charts and use existing hospital databases to allocate the direct costs of the medical care provided. They then consider the distribution of cost for the trial participants in comparison to the control group. Their results show a ten percent higher mean cost for trial

participants over their case-matched controls. They find that most cost-differentials incur in the first six months of the trial (Fireman et al. 2000 p141):

> *We focused on costs of care during the 1-year interval following enrollment in the trial. The modest differential in chemotherapy costs and total costs was entirely within the first 6 months. Among enrollees in trials, 94% of 1-year chemotherapy costs and 72% of 1-year total costs were incurred during the initial 6 months. Among control subjects, 83% of chemotherapy costs and 64% of 1-year total costs were in the initial 6 months. It seems likely that cost differentials during time periods beyond 1 year would be shaped primarily by recurrence and mortality.*

They suggest that economic evaluations of the benefits and costs of clinical trials should therefore be restricted to a one-year period early in the trial. The time period in the current study is greater than the one year time period recommended by Fireman et al. (2000) is selected for three reasons (1) it allows comparisons between trial stages, (2) it allows drawing on the health outcomes study conducted by CCRep using the same time period and (3) as this study involves a retrospective cohort design collecting data for the full eight year period involves little additional effort. A cohort design means that the population (in the current study these are CMDHB outpatients) is divided into two groups based on their treatment factors (Tay and Tinmouth 2007).

Bennett et al. (2001) report on five pilot case matched studies with 377 participants enrolled in phase II and phase III clinical trials. They find that cost estimates range from 10 percent lower to 23 percent higher for clinical trials than for standard medical care. In another case control study, Quirk, Schrag, Radzyne, Rubin, Nelson and Bosl (2000) find that 77 oncology trial participants have lower average treatment costs than their case matched controls.

Other studies calculate the drug cost avoidance for hospitals that run clinical trials. Watson (2006) maintains that DHBs can achieve significant savings by clinical research centres removing patients out of the public system for the duration of the trial. This has the potential to provide significant benefits from health cost avoidance though DHBs may not be aware of the cost avoidance that can be achieved. Watson (2006 p25) observes that:

> *The cost avoidance to a public hospital generated by enrolling patients in clinical trials should be a significant driver of increased demand by the hospital managers for clinical*

trials- something that seems to have not been registered on the financial radar of nearly all New Zealand hospitals.

Perrín and López (2008) assess whether HIV infected patients' participation in clinical trials influences drug costs. They extract data from the hospital pharmacy database. They then value: (1) cost saved (difference between cost per day during the trial and cost per day before study entry), (2) cost generated (difference between cost per day at the end of the trial and cost per day before study entry), (3) balance between cost saved and cost generated and (4) number of days that a patient received a drug once the trial was finished to generate cost, considering costs saved. They find that the cost of pharmaceuticals during participation in a clinical trial is lower than the cost prior to inclusion. However, they find that participation in a clinical trial generates extra cost once the trial has ended because the cost of pharmaceuticals is higher at the end of the study. One limitation of the Perrín and López study is the reliance on data pre and post-trial from the one group of trial participants rather than having a matched control group. They therefore were unable to account for differences in pharmaceutical costs, which were due to the natural progression of the illness. However, their study warrants further investigation. The current study will explore this further by considering cost in the follow-up period immediately after the trial has ended.

Sponsored clinical trials are changing with '*tighter budgets, more oversight, risks, financial pressures, and increased competition*' (Schmitt 2006 p751). Fireman, *et al.* (2000) show that to calculate the costs of clinical trials attention should be given to research infrastructure, data collection and other indirect costs as well as the direct medical care costs. However, when they review the literature, they find no studies that evaluate all of these factors. The economic outcomes strand of the current study will consider each of the types of costs identified by Fireman, *et al.* The micro-level BCA records data collection and direct medical costs borne by CCRep and the meso-level BCA records the indirect costs borne by CMDHB.

Researchers have been criticised for not taking a business-like approach when conducting trials (Silversides 2009). Wright, Roche, Smuck, Cormier, Cecchetto, Pilatzke and Pritchard (2005), report on two hypothetical clinical trials, which are distributed to nine cancer trial centres in Canada. Each centre then produces itemised budgets with per patient charges detailed for each trial. Thereafter each trial is separately considered as if sponsored by a federally funded cooperative group, and then as if sponsored by industry. The differences in charges are large

with the majority resulting from the estimates for professional support (nurse and physician) and radiology investigations. Estimated per patient charges for the first trial when considered as a federally funded cooperative group trial range from Canadian $1352 to $3082. Charges were much higher when considered as an industry-sponsored trial with estimated per patient charges ranged from $1700 to $7217. The second hypothetical trial results support these findings. Surprisingly no one centre consistently produced the highest or lowest estimates. These results prompted the authors to warn (Wright et al. 2005 p421):

> *For centres that negotiate specific per patient funding amounts with industry, this data would suggest a need to better understand the budgeting process and its link to appropriate resource identification to ensure appropriate funding is obtained. These issues are likely not unique to oncology.*

To be successful research co-coordinators must negotiate appropriate trial budgets and contracts that are not too demanding or risky for their site (Schmitt, 2006). With the costs of clinical trials rising (Johnston 2007; DiMasi 2008), clinical research centres need to identify the types of clinical trials they will be involved with, to avoid projects that may run at a loss (Collier 2009a). Ongoing staff training is a significant cost factor according to Schmitt (2006) who predicts that in the future certification examinations will become mandatory for all research staff, including investigators. Malakoff (2008) suggests clinical research sites should avoid protocols that include enrolment criteria that are so tight that it is difficult to find subjects who qualify. Getz (2007a p1) supports this view:

> *Investigators and site staff consistently report that managing site operations is difficult—particularly maintaining positive cash flow and profitability. Lead generation has intensified as competition for new study grants has increased. Study protocols have become more complicated and demanding. Patient recruitment and retention challenges have escalated. And the burden of regulatory compliance has become onerous and extremely frustrating*.

Many sponsors require investigators to indicate whether or not an adverse event or severe adverse event is related to a study drug, which can be difficult to do (Getz 2009). With poor clarity around the definition of unexpected adverse events and the variable incidence of severe adverse events safety reporting can be time consuming and therefore expensive though the magnitude of this workload has not been quantified (Getz 2009). The requirement that clinical

research sites go back through the entire consenting process whenever an amendment is made to the study protocol is another time concern for clinical research sites especially as protocol amendments are common (Getz 2007a). This can result in sites facing a large number of reports that must be forwarded to the institutional review board with no universal standards for reporting (Getz 2009). As compensation for the additional workload, some trial sites report that they are considering requiring additional compensation from sponsors of between US$500 and $750 per safety occurrence (Getz 2009). Recently the Clinical Trials Transformation Initiative (CTTI) announced a project aimed at improving the process of reporting and interpreting serious adverse events. (Clinical Trials Transformation Initiative 2009).

Compliance costs do not end when the trial ends. The maintenance of study records represents another challenge for sites. The long-term storage of records following the trial must be factored into overall costs (Getz 2007a). A 2003 Tuft Centre review finds that nearly ninety-five percent of clinical studies still use paper records (Kaitin 2003). Glass and DiFrancesco (2007) investigate the factors associated with efficiently run clinical trials. Seven pharmaceutical companies provide data for 262 phase III studies across 2047 sites. They find that better performing sites are those that begin enrolling participants and complete the enrolment process quickly. Better performing sites also have experienced clinical investigators including experience with the sponsor company. The costs in these studies are based on data from North America. New Zealand has a different medical system. Many of the trials conducted here are subcontracted from Australian research sites. The current study investigates the pattern of costs incurred by CCRep in undertaking clinical trials within a New Zealand public hospital that may be different from overseas.

Since the late nineties pharmaceutical industry sponsors have engaged ever-higher numbers of private physician practices and dedicated research centres to manage their clinical trials (Getz 2007b). These community-based for-profit investigative sites generally support Phase III programs a service, previously provided by academic institutions. Getz (2007b p1) describes the background to the change:

> *As these programs became larger and more complex and costly, industry sponsors grew tired of the inherent inefficiencies in working with academia, including protracted contractual and budget negotiations, bureaucratic and slow-moving institutional review boards (IRBs) and higher relative costs associated with poorer performance*.

The Tufts Centre for the Study of Drug Development report academic clinical offices conduct one-third of all industry sponsored clinical trials (Getz 2007b). The number of academic trials is low due to sponsored clinical trials providing low returns on infrastructure investment and limited institutional support. In addition, government-funded clinical research programs are seen as more prestigious than sponsored clinical trials according to Getz (2007b). The demand for foreign-based investigators and patients is increasing due to rising development costs and cycle times combined with the growing volume and scope of clinical trials (The Tufts Centre for the Study of Drug Development 2007).

The number of required participants in relation to the contract fee and the payment schedule may also affect profits. Options include paying the investigator at regular intervals or only upon completion of specific study milestones. The weighting of milestones may be equal or where the majority of the work occurs. The sponsor can also add an inflation adjustment for trials anticipated lasting longer than one year. Beal, Dean, Chen, Dragaon, Saulino and Collard (2004) advice researchers to review every trial once completed to identify any discrepancies between the estimated and actual costs.

This section has reviewed the published literature on the benefits and costs of conducting clinical trials from the perspective of the DHB or facility owner. The following reviews the literature on the benefits and costs for the New Zealand community.

THE BENEFITS AND COSTS FOR NEW ZEALANDERS

There is little information available on the economic benefits and costs of clinical trials from a macro-level perspective. The New Zealand government has supported clinical research since 1937 when it created the Medical Research Council, the precursor of the Health Research Council of New Zealand. A 2004 report by the Health Research Council of New Zealand evaluates clinical trial outcomes funded by The Health Research Council of New Zealand (2004). The report highlights six categories of outcomes: (1) fields of research, (2) establishment of networks, (3) clinical application of research, (4) uptake of research into practice, (5) dissemination of research and (6) building research capacity. New Zealand newspapers also provide some insight to the benefits of conducting clinical trials in New Zealand (see for example New Zealand Press Association 2008; Flagler 2005).

Watson identifies five key benefits to New Zealand society in undertaking clinical trials: (1) immediate economic benefits associated with oversees sponsors investing in New Zealand (2) building New Zealand's reputation in international research circles (3) access to more resources to enable the up-skilling of New Zealand health researchers (4) providing stimulating work within New Zealand for researchers and therefore stopping the current brain-drain (4) receiving pharmaceutical company sponsorship money for not-for-profit organisations and (5) attracting clinical trials in areas that the New Zealand government targets as priority diseases.

Conducting clinical trials in New Zealand provides the assurance that the new drugs have been tested on and are safe for use by New Zealanders. Giuliano, Mokuau, Hughes, Tortolero-Luna, Risendal, Ho, McCaskill, Stevens and Prewit (2000) find that white, married, middle class, highly educated males are the group most often represented in clinical cancer trials in America. This finding prompts Robinson and Trochim (2007) to suggest that the development and testing of all new drugs include individuals from diverse racial and ethnic groups. They feel this is important due to the large racial and ethnic variation in disease incidence and mortality rates. This finding suggests that to gain the full benefit from clinical trials conducted in New Zealand, clinical trial participants should represent New Zealand's diverse cultural base.

To maintain and expand the clinical trials industry in New Zealand Watson (2006) asserts that the New Zealand government must reform PHARMAC and its highly restrictive policies of pharmaceutical access. The exact nature and costs of this improvement have not been calculated. An estimation might be the NZ$2 billion which are savings from PHARMAC's policies in the first ten years of operation (PHARMAC n.d.). Another possible way to estimate costs is to examine the costs of other countries that have introduced incentives to encourage sponsored clinical trials. The Australian government through the Pharmaceuticals Partnership Program (P3) aims to increase clinical trials by offering participating companies thirty cents for each additional dollar they spend on eligible research in Australia to a maximum grant of A$10 million (Australian Government, 2004). New Zealand has yet to follow this lead.

This section has reviewed the literature relating to the benefits and costs of clinical trials to New Zealanders. He research suggests that potentially sponsored clinical trials have an important role in New Zealand's health system. They may reduce costs for New Zealand DHBs and allow faster access to new drugs. Given that investment in health research has been found to produce 'exceptional returns' (Access Economics 2008a) and that clinical trials are an important

component of health research, further study from the macro-level perspective is likely to be informative.

The benefits and costs to the international community is the subject of the final review.

THE BENEFITS AND COSTS FOR THE INTERNATIONAL COMMUNITY

Clinical trials around the world feed information into the global knowledge base, although the benefits of clinical research among countries vary according to their societal values (Buxton et al. 2004). The review finds little information specifically on the benefits and costs of clinical trials as they relate to the international community. However, the review finds several studies investigating the benefits and costs of medical research. Medical research, often referred to as health and/or medical research, has a wider scope than clinical research. Health research includes all initial research leading up to and including clinical trials. Medical research provides both a private value and a public value. The individual consumes the private value over their lifetime. To calculate the social value economists use both the 'current and expected future populations benefit from the change' (Murphy and Topel 1998 p16). The social value is therefore likely to be large.

Some studies quantify the benefits from health gains to justify investment in medical research (Buxton et al. 2004). Difficulties can arise in calculating the benefits of medical research in particular in establishing the nature of the link between mortality rates and health improvements. There are times when mortality is reduced without health changes, for example, with accident prevention strategies and times when improved health does not reduce mortality for example knee replacement surgery (Murphy and Topel 1998). Medical advances decreasing the mortality from one disease may add value through reducing the mortality from other diseases, for example, '*A reduction in mortality from heart disease raises the value of advances against Alzheimer's because people are more likely to survive to old age*' (Murphy and Topel 1998 p15). Some international studies show high returns from investing in medical research. In a United States of America (USA) based study, Murphy et al. (1998) investigate the economic value of improvements in life expectancy and quality of life between 1970 and 1990. They estimate them to have a value of approximately $1.5 trillion/year. They assign one third of those gains (about $500 billion) to health research and conclude that these economic returns far exceed the costs of

the health research that contributed to them by more than 20-fold. They develop an economic value of health and life expectancy model to estimate savings from future health care innovations. They calculate the savings as substantial, for example, finding a way to eliminate heart disease mortality in the USA is worth US$48 trillion, research achieving a one percent reduction in deaths from cancer yields US$500 billion while a cure is worth US$500 billion. Access Economics (2003) show similar high returns In Australia. They report an eight-year increase in life expectancy between 1960 and 1999 worth A$5.4 trillion dollars. They update their study in 2008 and demonstrate continued high returns in health investment.

THE VALUE OF CLINICAL TRIALS: THEORETICAL MODELS

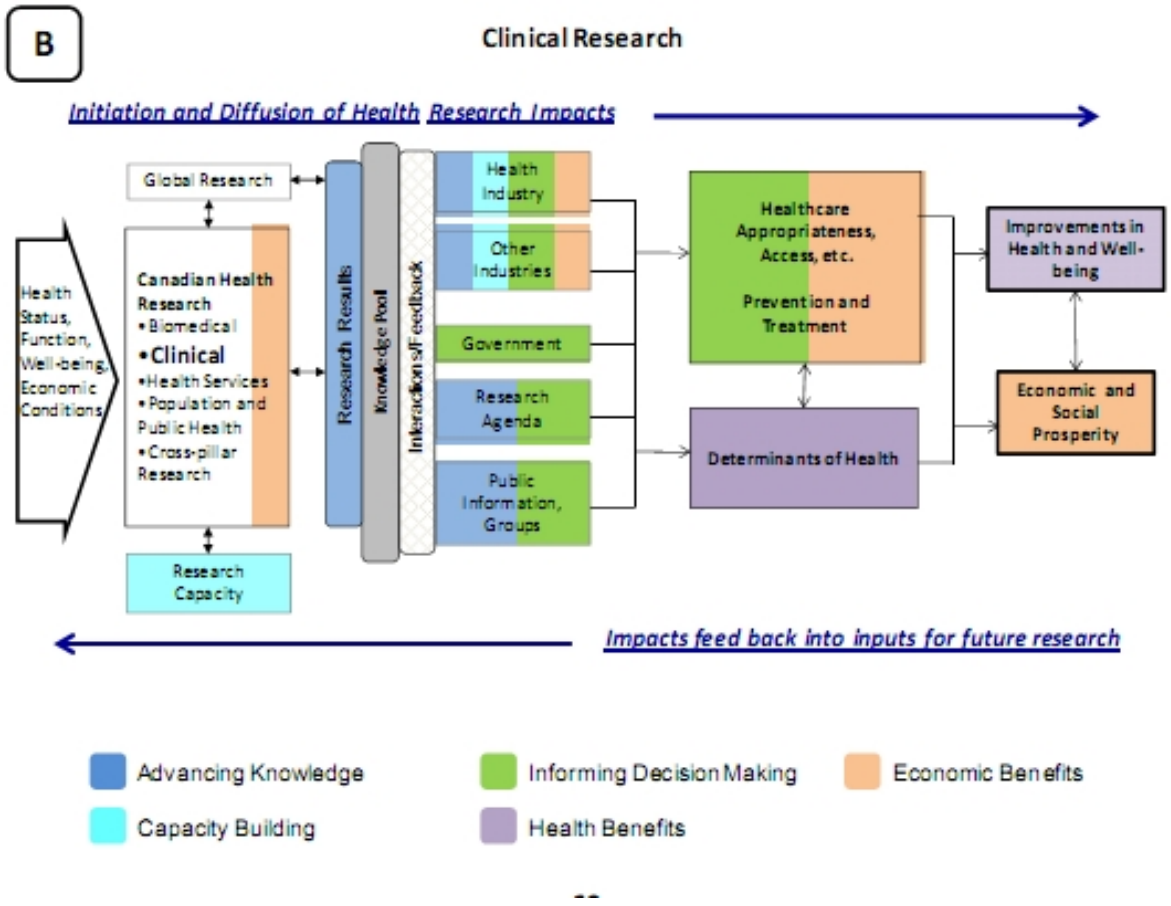
The review above identifies a wide range of costs and benefits that impact on the multiple stakeholders involved with clinical trials. Theoretical models can be used to group trial benefits and costs and provide different constructions of the clinical trial nexus This section identifies several theoretical models that support the understanding of the value of clinical trials. The review maintains an international perspective by including views from the United Kingdom and Japan. The first models this review considers take a broad focus and examine the benefits that arise from investing in health research at a macro-level. The Ono and Kodama (2000) model takes a societal view on the benefits and costs of clinical trials and draws on experiences in Japan. The section reviews two leading models using a micro-level view. The Braunholtz Edwards and Lilford Trial Effects Model (2001) explore the short-term benefits of clinical trials. Finally, Mueller's (2004) contingency model provides an understanding of participant's reason for their involvement in clinical trials.

MACRO-LEVEL MODELS

Although, the current study considers sponsored clinical trials it briefly discusses here the wider field of medical research as many benefits and costs apply to both. The current study investigates benefits and costs at the macro or national level, the meso or local level and the micro or individual level. Most models evaluate health research at the macro-level (Hage 2009). Macro – level approaches to health research review tend to fall into two groups (1) 'top-down' econometric evaluations and (2) 'bottom-up' methods to measuring return on investment (Shiel

and DeRuggerio 2009). The Lasker Foundation uses a top-down approach to economic evaluation to estimate the value of the United States return on investment on health research. They monetise both changes in life expectancy and quality of life to give an estimated return between the years 1990 and 2000 at about $500 billion (Funding First 2000). Buxton and Hanney (1996) use a bottom-up approach in their payback model. This involves the tracking of new knowledge beginning with the researcher adding to a knowledge pool and then to secondary outputs and adoption to tracking outcomes.

FIGURE 3-2 IMPACTS OF APPLIED CLINICAL RESEARCH (SOURCE: PANEL ON RETURN ON INVESTMENT IN HEALTH RESEARCH, 2009A, P 69).



The Canadian Academy of Health Sciences (Panel on Return on investment in Health Research 2009a) modifies the Buxton et al. (2004) payback model to allow the tracking of impacts in five categories: (1) advancing knowledge, (2) capacity building, (3) informing decision-making, (4)

health benefits, and (5) broad economic and social benefits. Figure 3.2 shows that the model and outcomes when applied to clinical research. The model identifies four groups where impacts might occur (1) the health industry, (2) other industries, (3) government, (4) research decision-makers, or public groups — and follows them through stages of adoption to final outcomes in (1) health, well-being and social or (2) economic prosperity. While this model has potential to provide a framework for evaluating research outcomes at the macro level it is still new and requires further study to ascertain its application across a range of research environments. Chapter 7 of this thesis compares this classification to the results of the current study.

A SOCIETAL PERSPECTIVE.

TABLE 3-4 BENEFITS AND COSTS OF CONDUCTING A CLINICAL TRIAL (SOURCE: ONO AND KODOMA 2000)

Party	Benefits	Costs
Participant	Value of volunteerism (e.g. altruistic behaviour) Value of positive outcome (Depending on allocation to active or placebo group) 1. life saved productivity saved Value of closer relationship with medical staff	Direct costs 1. changes in use of healthcare resources (e.g. consumption of drugs and services, treatment of possible adverse drug reactions)changes in use of patient time (e.g. travel and waiting time of frequent visits, time for informed consent process)Productivity costs
Sponsor	Value of clinical data 1. study reports published articles Know-how or positive externality	Resources allocated to a clinical trial (e.g. monitors, auditors)
Investigator	Value of clinical data 1. study reports published articles Prestige	Direct costs changes in use of healthcare resources changes in use of investigator time Productivity cost
Public (patients)	Value of therapeutic effects of marketed drugs (occurs downstream); should be discounted; determines the value of data for the sponsor and the investigator, these values should not be double counted	

Ono et al. (2000) investigate the benefits and costs of conducting clinical trials in Japan from the perspective of Japanese society (Table 3.4). They identify three types of benefits (1) benefits to practitioners and trial participants gained during the course of the clinical trial (2) benefits from research publications and other research outputs (3) immediate and future benefits that arises on introduction of the new drug to the market.

Ono et al. calculate the cost of resources used and take into account any opportunity costs. This approach begins to recognise the impact clinical trials have on society rather than only those directly involved, however it is incomplete, as it takes into account neither the jobs created by clinical trials nor the effect of overseas sponsor's investment in the local economy.

MICRO-LEVEL MODELS

Micro-level models consider the benefits resulting from the conduct of clinical trials. There follows two of these models next: a model constructed by Braunholtz et al. (2001) who classify trial effects at the participant level and reviews then research by Mueller (2004) on why participants volunteer for trials.

BRAUNHOLTZ, EDWARDS AND LILFORD

Braunholtz et al. (2001) investigate the effects of participation in clinical trials. They summarise trial data to determine whether clinical trials are beneficial or detrimental to participants. Their findings suggest that well conducted trials tend to benefit the participants on average and do not in most instances result in harm. Braunholtz et al. identify five trial effects that may influence differences between trial and non-trial groups: (1) treatment effect, (2) protocol effect, (3) care effect, (4) Hawthorne effect and (5) placebo effect. Brief descriptions of these effects appear in Table 3.5. Trial effects can result in benefits and costs for the participants involved in the clinical trial and also for those who are not involved. Braunholtz et al. express concern about the ethical implications of trial effects (p 223):

> *The spirit of the Helsinki Declaration demands that physicians do their best for each individual patient in their care, so it could be argued that patients outside trials should not systematically receive inferior care as a consequence of not being in a trial. Certainly the Helsinki Declaration precludes using a protocol/Hawthorne effect as an inducement to persuade patients to participate in trials. Any such effect should therefore be*

unintended. Even if a systematic advantage is not intended, the consequences of it remain the same.

They suggest redressing treatment effects by giving all eligible patients access (if they choose) to both the risks and benefits of clinical trials by allowing all patients entry into trials so that trials become routine treatments. Ensuring all treatments whether or not they involve patients enrolled in a trial utilise protocol conditions addresses Hawthorne, care and protocol effects. Although this theory is too narrow to capture the range of benefits and costs explored in the current study, the classification of trial effects provides a useful framework for analysis.

TABLE 3-5 DIFFERENCES AMONG COMPARISON GROUPS THAT MAY CONTRIBUTE TO A TRIAL EFFECT (ADAPTED FROM: BRAUNHOLTZ ET AL. 2001 P218)

Trial Effect	**Difference**	**Comparison Groups**
Treatment Effect	Would occur if treatments used in trials were better or not as good as standard alternatives.	Placebo vs. treatment group
Protocol Effect	Differences in regimens of main treatments for example rigorous trial protocol vs. less rigorous treatment guidelines.	Participants vs. others in standard care
Care Effect	Differences in incidental aspects of care, e.g. extra nursing cover or extra follow-up for trial patients.	Participants vs. others in standard care
Hawthorne Effect	Changes in patient or clinician behaviour (other than is prescribed in the trial protocol) due to involvement in trial, e.g. due to the feeling of being "observed".	Participants vs. others in standard care Recruiting clinicians vs. non-recruiting clinicians
Placebo Effect	Psychologically mediated effects due to being enrolled in a clinical trial, e.g. there may be differences between patients who generally agree to participate and those who tend to refuse.	Participant vs. refusing patients Participants and refusing patients vs. non invited patients

MUELLER (2004) CONCEPT OF CONTINGENCY.

One approach to understanding the perceived benefits from participating in clinical trials is to examine the motives and perspectives of potential trial participants. Mueller (2004) asks participants with human immunodeficiency virus (HIV) how they decide to enrol in a clinical trial and then uses what she calls '*the concept of contingency* (2004 p705) to illustrate their decision making process. Mueller defines contingency as (p707)*'an identification and interpretation of uncertainty and the work or effort to control or manage that uncertainty by giving (or not giving) consent or to partake in clinical trials'* Mueller applies the concept of contingency in a medical context to describe a means of managing the unanticipated and most challenging aspects of healthcare. Mueller suggests participants consider three kinds of contingencies before enrolling in a clinical trial (1) clinical (2) social and (3) technical.

Clinical contingencies assist potential participants to deal with failing health and limited care options. Mueller identifies clinical trials as a contingency for coping with the uncertainties that a diagnosis causes. Participants engage a clinical contingency when they regard the available treatment outside of the trial as unsatisfactory.

The second group of contingencies Mueller calls social contingencies. Social contingencies take three forms, altruism, trust and structure. Participants use an altruistic contingency view when they enrol in a trial to help others and ultimately help themselves. Trust in the advice given by the referring physician may influence the potential participant to follow the 'expert' advice and enrol. Structure provides an event or purpose to the often-unfocussed lifestyle of people with disabilities.

Finally, prospective participants use technical contingencies when they enrol in a trial to obtain technical information about their disability not otherwise available to them. Patients participate in a trial as a strategy that will allow the collection of information needed to make decisions about their on-going treatment. The concept of contingency provides a good starting framework for understanding the decision making process for those considering enrolling on a trial. As it is new, further research is needed to confirm its flexibility and comprehensiveness.

This section has outlined the theoretical models that can be used to understand the outcomes of clinical trials. It has explained the micro, meso and macro- levels of analysis used in the thesis. In doing so, it justifies the value of the multi-method, quantitative and qualitative approach used in the current study.

CONCLUSION

This chapter has reviewed the empirical literature on the value of clinical trials from the perspectives of the multiple stakeholders. Promotion of the potential benefits of clinical trials must always be tempered by discussions of potential costs – for the trial sponsor there are seldom short-term gains to be made, and for trial participants there may be health risks arising from participation. It is important to develop an accurate method to measure the current and future value created by clinical trials in New Zealand. Currently there is a paucity of good data and without which DHBs cannot make good planning decisions.

Recent literature reveals little information on the benefits and costs related to clinical trials in New Zealand, whether they relate to health outcomes, stakeholder perceptions or economic outcomes. The modest amount of available literature suggests there may be health, social and economic advantages for the research unit, the health board and New Zealand society arising from actively encouraging sponsored clinical trials within publicly funded hospitals.

Watson (2006) provides some insights that the current study will further explore. International studies have produced a variety of results on the benefits and costs of clinical trials. For some stakeholder groups abundant but occasionally conflicting information is available (for example the pharmaceutical companies). For other stakeholder groups very little information is known (for example family and caregivers). The available literature suggests that trials on average and if conducted well tend to benefit the participants and do not, in most instances, cause harm. These studies suggest that the conduct of clinical trials offers potential benefits to trial participants and cost savings to the New Zealand health sector.

The theoretical models reviewed in the second part of this chapter provide various interpretations of the clinical trial nexus. They describe different ways to assess the benefits and costs of clinical trials and provide a framework for understanding the empirical research reviewed in the earlier section of the chapter. An analysis of the benefits and costs of clinical trials can focus on different aspects or levels.

Table 3.6 summarises the findings from the literature review. The literature provides some insight into the potential benefits and costs of conducting clinical trials within a New Zealand public hospital. The benefits and costs of clinical trials appear multi-layered and dependent on the stakeholder perspective taken. The review identifies benefits for stakeholders in the conduct

of clinical trials including the provision for training and development for medical staff, better medical outcomes for participants and savings from treatment cost avoidance for DHBs. It also identify some potential costs associated with trials including the high workloads for researchers and DHB staff, additional costs of transport for participants and increased use of testing facilities.

Most of the reviewed research considers benefits and costs from the view of a health professional. Although useful, this can lead to biasing the research towards a professional's view of the world rather than that of the user (Kitson 2002). Hanson et al. (2006) suggest that when conducting research all forms of evidence is equal regardless of who presents it. They believe genuine collaboration between researchers, patient and caregiver groups 'means acknowledging the importance of differing forms of 'evidence' and expertise' (Hanson et al. 2006 p340). Although the papers reviewed here are diverse in nature, it is evident that many of the issues regarding clinical trials are similar across study boundaries.

A second way to structure the review of empirical research is by its macro, meso or micro-level focus. Macro, meso and micro levels studies analyse clinical trials at different levels and use several kinds of information. Macro-level studies consider the costs and benefits to society. There is little information available on the economic benefits and costs of clinical trials from a macro-level perspective. In the few studies identified the review finds the sources of data are most often official, statistical data on health, health care utilisation and health care resources. They apply either a 'top-down' or a 'bottom-up' method to measure benefits and costs and employs economic modelling to estimate economic outcomes.

Studies at the meso-level consider costs and benefits from the perspective of the organisation. Comparisons are made concerning groups of patients either enrolled in a trial or receiving standardised care. Costs and benefits can be measured by health care utilisation/costs or patient outcomes. Sources of data might be statistics on health, health care utilisation/costs.

Studies at the micro-level identify the immediate benefits and costs at the clinical level. Benefits and costs can be studied using data from claims for reimbursement or data from other accounting records. The micro-level studies presented in this review provide insight into the scope of benefits and costs that may arise from clinical trials

The current study applies a macro, meso and micro level structure in the planning, data collection and presentation of the quantitative aspects of the current study reported in Chapter 6. The following chapter discusses the methodology influenced by the review of the literature presented here.

TABLE 3-6 SUMMARY OF BENEFITS AND COSTS OF CLINICAL TRIALS IDENTIFIED IN THE LITERATURE.

TRIAL PARTICIPANTS	
BENEFITS	**COSTS**
Access to the latest development in pharmaceutical care at no cost (Watson 2006) Extensive medical review process (Watson 2006) Direct health benefits (Hanney et al. 2004). Perception of being cared for by experts (Burnet et al. 2004) Treatment effects, protocol effects, care effects, Hawthorne effects: changes in patient or clinician behaviour (Braunholtz et al., 2001) Control over clinical uncertainties (Mueller 2004) Opportunity to do "something for others" (Mueller 2004) Education about illness with associated behaviour changes towards self-management (McGuinness 2007) Structure to mundane lifestyle (Mueller 2004, Moore 2001) Closer relationship with medical staff (Ono et al., 2000) 'Fascinating' and 'interesting' experience (Burnet et al., 2004). Personal satisfaction and a sense of purpose (Cox 1999). An enhanced sense of hope and altruistic feelings (Burnet et al., 2004).	Perception of being used as a guinea pigs (Ellis 2000) Direct costs of healthcare resources (e.g. consumption of drugs and services, treatment of possible adverse drug reactions) and time (e.g. travel and waiting time of frequent visits, time for informed consent process) (Ono et al. 2000) Productivity opportunity costs (Ono et al. 2000) Interferes with returning to 'normal life' stress of car-parking and child care (Burnet et al. 2004) Less flexibility (United States General Accounting Office 1999) Needs may become subordinate to the conduct of the clinical trial (Lee 1999) Painful medical procedures (Malakoff 2008) Concerns about treatment toxicity (Ellis 2000 Changes in regular medical staff (Blackburn et al. 1994)

FAMILY MEMBERS AND COMMUNITY CAREGIVERS	
BENEFITS	**COSTS**
Pharmaceutical industry sponsorship of community support organisations (Watson, 2006) Greater knowledge about specific disabilities and greater chance of new cures (O'Connell et al. 2006) More involvement in health care (Bastian 1998).	Time spent assisting the participant in the home during trials and transporting participants to and from appointments. (Hynes et al. 1999) Costs of producing participant information about trials (O'Connell et al. 2006)
STAFF MEMBERS AND RESEARCHERS	
BENEFITS	**COSTS**
Education and experience with new treatments and technology, increased research opportunities, networks with international clinicians (Watson 2006) May apply the results from clinical trials in own practice (Ketley et al. 1993) Greater job satisfaction (Bell et al. 2006) Clinical data, published papers and prestige (Ono et al. 2000).	Time required to run trial (Roche et al. 2002, Sale 2007, Getz 2007a) Uneasiness over ethics of clinical trials, possible conflict of interest between research and clinical roles (Sale 2007) Feelings that work is unrecognised (Sale 2007) Direct costs of healthcare resources and use of researcher time (Ono et al. 2000). Sponsored trials can be boring and unchallenging with limited opportunities for researcher input (Scheifele 1997) Restrictions on publications (Scheifele 1997) Conflict between a physician-scientist's devotion to the promotion of health for the individual patient and allegiance to the outcome of clinical research (Lee 1999)
PHARMACEUTICAL INDUSTRY	
BENEFITS	**COSTS**
Value of clinical data, study reports and published articles (Ono et al. 2000) Know-how or positive externality (Ono et al. 2000)	Cost of new drug development US$802 million (DiMasi et al. 2003) Cost of new drug development US$479 - $1,134

	million (Adams et al. 2006) Resources allocated to a clinical trial e.g. monitors, auditors (Ono et al. 2000) Finding sites for trials up to US $20,000 (Malakoff 2008) Recruiting subjects – delays cause loss up to US$1.8 million per day (Reichert et al. 2002) Medical costs of participants (Watson 2006) Costs of trial procedures(Watson 2006)
DHBS AND FACILITY OWNERS	
BENEFITS	**COSTS**
Hospitals with better health care and lower mortality rates (Majundar et al. 2008) Development of research informed policies (Hanney et al. 2004). Treatment cost avoidance: radiology, clinical input, overhead expenses, and significantly reduced and in some cases no pharmaceutical cost (Watson 2006, LaFleur et al. 2004). Research agenda can be set by the organisations needs (Lomas 2003). Helps build centres of excellence (Australian Government 2004). Increases uptake of new medical practice (Hanney et al. 2004).	Accounting and payroll, purchasing, building maintenance, rent for laboratory/office space, equipment depreciation, administration costs, basic utilities, staff training and site initiation visit, IRB fees, start-up payment, personnel fees, monitoring and serious adverse event reporting, mailing and shipping, record storage, equipment and supplies, laboratory fees, radiology fees, pharmacy fees, patient follow-up and travel (Beal et al. 2004).
NEW ZEALAND SOCIETY	
BENEFITS	**COSTS**
Establishment of networks, clinical application of research, uptake of research into practice, dissemination of research and building of research capacity (The Health Research Council of New Zealand 2004). Improves the knowledge economy by building an effective and efficient research sector (Australian Government 2004)	To increase number of clinical trials New Zealand needs to reform PHARMAC policy (Watson, 2006) PHARMAC saved New Zealanders $2 billion in first 10 years of operation (PHARMAC nd) Subsidies to improve Volume of clinical research investment and match Australia 30 cents per dollar invested (Australian Government 2004)

Builds international reputation for excellence, attracting and retaining researchers and securing investments from industry and oversees. (Australian Government 2004) Helps build research infrastructure (Watson 2006) Job creation and increased tax base due to higher paid jobs created (Commonwealth of Australia 2004) Cost avoidance from reduced illness (Access Economics 2003) Oversees revenue as a result of international funding of clinical trials (Watson 2006).	

INTERNATIONAL COMMUNITY	
BENEFITS	**COSTS**
Improvements in living standards and life expectancy (Access Economics 2003) Reduced mortality and morbidity (Wisconsin Assoc of Biomedical Research 1995) Research achieving a one percent reduction in deaths from cancer in the USA would yield $US500 billion while a cure is worth $US500 billion.(Murphy et al. 1998) Australian health research achieved an eight year gain in Australians life expectancy between 1960 and 1999 worth $A5.4 trillion dollars (Access Economics 2003 Improves performance of health systems (Pardes et al. 1999) Helps target future research and builds a knowledge generation (Hanney et al. 2004). Therapeutic effects of marketed drugs (Ono et al. 2000)	Consumes resources needed for other areas of health care (Woolf et al. 2005) Market forces mean drug development focus resources on diseases of the rich not those of the poor. (Ridley *et al.* 2006).

4. RESEARCH METHODS

The research question is: 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?' In seeking to answer this question, the thesis analyses an empirical study of the value of conducting clinical trials in a publicly funded New Zealand hospital and reports the results. The thesis thus far has introduced the study topic, established the theoretical foundations and provided a synthesis of the empirical research that informs the current study. This chapter provides a detailed description of the design and execution of the study, along with a justification of the chosen methods.

The chapter proceeds as follows. The next section presents an overview of the study. The following section identifies the worldview that provides the foundation for the research. The next section explains the methodology and provides justification for the methods used in the research. Following that is a section that presents the research design; the methods used and highlights the choice of sampling techniques, data collection and analytic methods for the economic and multiple stakeholder perception strands. The chapter concludes by describing the ethics approval process and summarising the combined potential of the two strands to produce a strong analysis of clinical trials.

The definitions of the terms in this study are: (1) a worldview is a belief about what knowledge is and how it is constructed (Morgan 2007); (2) methodology is an '*analysis of the assumptions, principles, and procedures in a particular approach to inquiry*' (Schwandt 2001 p161); (3) research design is a '*procedure for collecting, analysing, interpreting and reporting data in research studies*' (Creswell and Plano Clark 2007 p58) and (4) methods are the tools and techniques used to gather data. Bechhofer (1974 p73) observes:

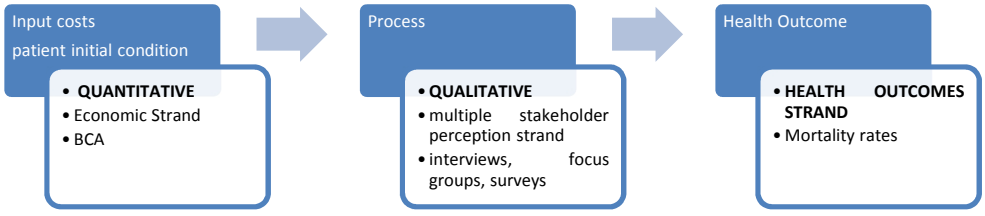
> *the research process is not a clear cut sequence of procedures following a neat pattern, but a messy interaction between the conceptual and the empirical world, deduction and induction occurring at the same time.*

The method for the current study was to a certain extent an evolving one, which took shape as the study progressed.

STUDY OVERVIEW

The preceding chapters reveal the variety of ways scholars use to measure value. Most measurements of value and value creation are dependent on a profit-making motive. Value measurement in the not for profit sector is more challenging for two reasons, firstly the lower importance given to value creation and other financial indicators. Furthermore, the not for profit sector is characterised by complex systems and multiple intangible variables which are difficult to measure (Boselli, Cesarini and Mezzanzanica 2011). Porter (2008) advances a framework to measure value in the health sector. The researcher employs the empirical study developed in this chapter to evaluate clinical trials in a publicly funded New Zealand hospital. The current study is based on Porter's (2008) approach to value discussed in chapter 2 and includes the dimension of stakeholder perceptions of the clinical trial process. The current study adopts the view that multiple outcomes jointly constitute value, and considers outcomes from several different perspectives.

FIGURE 4-1 RELATIONSHIP BETWEEN CURRENT STUDY AND PORTER'S (2008) APPROACH TO MEASURING VALUE IN HEALTHCARE.



As discussed in chapter 1, the current research builds on a health outcomes study that involves a retrospective cohort study of changes in trial participants' health status and mortality rates. This health outcomes strand is the equivalent of the health outcomes identified in Porter's framework (see figure 2.2 in chapter 2). The focus of the economic outcomes strand of the current study is on cost and cost avoidance and therefore links to the cost side of Porter's (2008) value equation. Porter's (2008) framework defines the outcome or benefit of medical interventions as improved patient health. However, medical interventions may also generate wider benefits to other stakeholders, for examples family and caregivers reduction in time spent caring for the patient or

the reduction in the risk of treatments for the wider community. In partial recognition of this Porter (2008 p166) observes that "*service experience can be important to good outcomes"* The current study incorporates the non-quantifiable outcomes many of which focus on the treatment process into a qualitative strand that investigates stakeholder perceptions of clinical trials (see figure 4.1). CBA is a useful method of measuring the value of items easily quantified. This study therefore adopts CBA as one of the methods used to measure the value of clinical trials.

WORLDVIEW

In developing the research design, the r seeks to articulate worldview and methodology. Positivist versus constructivist debates abound in the literature (Bryman 2007b) and researchers have historically opted for either a positivist worldview, associated with quantitative methods or a constructivist worldview associated with qualitative methods (Doyle, Brady and Byrne 2009). '*The different world views they reflect imply different grounds for knowledge about the social world*' (Morgan and Smircich 1980 p493). Positivists believe that only phenomena that are observable and measurable are valid. The positivist researcher tries to maintain an independent stance and observe strong objectivity (Hussey and Hussey 1997). Positivists believe in a singular reality (Creswell and Plano Clark 2007). Objective facts are a means to constrain subjective beliefs (Smith 1983). Thus results obtained using a positivist approach are regarded as universal and are able to be generalised across time and in different contexts (Morgan 2007). Positivists use deductive reasoning where a hypothesis is established and then tested. Deductive reasoning is an upfront assumption about what the researcher will find from the results of a study (McGivern 2006). It moves from a general idea about what might happen to a specific observation to see if it really does happen (McGivern 2006). Positivists strive to eliminate bias and write in a formal style using agreed definitions (Creswell and Plano Clark 2007). Morgan and Smircich (1980 p493) summarise this world view and state that positivists have

> *an emphasis on the empirical analysis of concrete relationships in an external social world. It encourages a concern for an 'objective' form of knowledge that specifies the precise nature of laws, regularities, and relationships among phenomena measured in terms of social "facts".*

In contrast, constructivism involves subjectivity, which requires the distance between the researcher and the subject to be minimised (Morgan 2007). Constructivism is sometimes known as post-positive, naturalistic enquiry or interpretive enquiry (Creswell 1994), it incorporates the assumption that beliefs determine what should count as facts (Smith 1983), has multiple realities and seeks to illustrate different perspectives (Creswell and Plano Clark 2007).The approach is normally regarded as specific and context dependent (Morgan 2007). It uses inductive reasoning, building theory during the research process and aims for a deeper understanding from a small sample (Doyle et al. 2009).

During the study, data are collected from the participants, sites and general principles that apply to the subject under study are identified (McGivern 2006). The process involves moving from specific to the general (McGivern 2006). The constructivist approach recognises the bias of the researcher allowing the researcher to discuss their interpretations (Creswell and Plano Clark 2007). The researcher writes the report in an informal style (Creswell et al. 2007). The emphasis is therefore different. As Morgan and Smircich (1980 p493) suggest, a constructivist

> *emphasizes the importance of understanding the processes through which human beings concretize their relationship to their world. This phenomenologically oriented perspective challenges the idea that there can be any form of 'objective' knowledge that can be specified and transmitted in a tangible form, because the knowledge thus created is often no more than an expression of the manner in which the scientist as a human being has arbitrarily imposed a personal frame of reference on the world, which is mistakenly perceived as lying in an external and separate realm*

Table 4.1 summarises the differences between these two worldviews. While purists argue that positivism and constructivism cannot be combined (Smith and Heshusius 1986, Lincoln and Guba 2000), others suggest that these world views exist on a continuum and that claimed distinctions are less obvious under scrutiny (Bryman 2001, Brannen 2005). Morgan and Smircich (1980) support the continuum approach to worldview. Morgan and Smircich (1980 p493) describe the changes to world view or epistemology that occur as a move is made along the continuum from positivism to constructivism:

> *the epistemology of extreme positivism, derived from a mechanical conception of the universe as a closed structure, gives way to an epistemology emphasizing the need to*

understand process and change. It is a change in epistemology that reflects a move away from a conception of the world as a machine, or closed system, to a conception of the world as an organism, an open system.

TABLE 4-1 COMPARISON BETWEEN CONSTRUCTIVISM AND POSITIVISM (ADAPTED FROM: GUBA 1985, CRESWELL AND PLANO CLARK 2007, MCGIVERN 2006).

	Constructivism	**Positivism**
Epistemology: the relationship of the knower to the known; the nature of knowledge and its justification	Closeness Subjectivity Knower and known are interactive and inseparable	Distance Objectivity Knower and known are independent, a dualism
Ontology: The nature of reality, being and truth	Multiple realities	Singular reality
Axiology: the role of values	Biased	Unbiased
Connection of theory and data	Induction	Deduction
Inference from data	Context	Generality
Language used in reporting research	Informal	Formal

Taking the continuum view further, an alternative to a constructivist or positivist approach is pragmatism (Johnson and Onwuegbuzie 2004, Morgan 2006). Pragmatism considers the empirical and practical consequences when evaluating ideas and researchers consider what works best when establishing the research design (Johnson and Onwuegbuzie 2004, Creswell and Plano Clark 2007). The pragmatic researcher uses what M organ calls abductive reasoning, which relates to the way the researcher freely moves between inductive and deductive reasoning. In practice, this means that a researcher converts observations into theories and then acts on them as an assessment of those theories (Morgan 2006).

The pragmatic researcher also moves comfortably between subjectivity and objectivity which Morgan has labelled being in a state of intersubjectivity. Thus when using a pragmatic approach a researcher works with the belief that there is a single real world but individuals will have their own interpretation of that world (Morgan 2006). Pragmatism challenges the boundaries of what can be done with research results by exploring how at least some of the new knowledge can be

applied in new circumstances. It thus avoids the all or nothing approach of the positivist and the constructivist (Morgan 2007).

TABLE 4-2 DIFFERENCES BETWEEN CONSTRUCTIVISM, PRAGMATISM AND POSITIVISM (ADAPTED FROM: HOSHMAND 2003, MORGAN 2007, CRESWELL AND PLANO CLARK 2007).

	Constructivism	**Pragmatism**	**Positivism**
Nature of reality	Multiple realities	Singular and multiple realities	Singular reality
Connection of theory and data	Induction	Abduction	Deduction
Relationship to what is being investigated	Closeness	Practicality	Distance
Relationship to research process	Subjectivity	Intersubjectivity	Objectivity
Role of values	Biased	Multiple stances	Unbiased
Inference from data	Context	Transferability	Generality
Language used in reporting research	Informal	Formal or informal	Formal

Using a pragmatic worldview Creswell, (2008 p 11) suggests

> *individual researchers have a freedom of choice. In this way, researchers are free to choose the methods, techniques, and procedures of research that best meet their needs and purposes.*

This allows the researcher the ability to move freely between the two strands of the mixed methods study. The researcher adopts methods that work best in considering empirics, analysis, and conclusions when collecting and analysing data and reaching conclusions. Chapter 2 of this thesis reviewed the empirical literature around the costs and benefits of clinical trials. This review revealed the dominance of quantitative research with minimal recognition of the value that qualitative studies may add. By adopting a mixed methods approach this study seeks to address this imbalance.

The next step in the research process is the choice of methodology.

METHODOLOGY

Methodology provides justification for the methods of a research project (Carter and Little 2007). Researchers have traditionally chosen between qualitative or quantitative methodologies. Mixed methods research emerged as an evolution in the late 20th century. Tashakkori and Teddlie 2003) suggest publications promoting mixed methods research began to emerge in 1988 with writers such as Bryman (1988), Greene, Caracelli and Graham (1989), and Creswell (1994). Qualitative methodology derives from constructivism and uses inductive reasoning to understand the meanings individuals give to phenomena (McGivern 2006). Qualitative methods include focus groups, in-depth interviews, and observation to obtain detailed, context-rich findings presented in words, matrices and pictures (McGivern 2006, Curry, Nembhard and Bradley 2009). Researchers ask open-ended questions to help gain an in-depth understanding of a single idea or phenomenon (Creswell and Plano Clark 2007).Quantitative methodology applies a positivist paradigm to statistically test hypotheses in experimental and natural settings (Curry, Nembhard and Bradley 2009).

Quantitative research methods include a range of techniques that are used to gather measurable data of a quantity and quality to support empirical analysis using statistical methods (Anderson and Widener 2007) and may include surveys and interviews in which closed questions are asked of participants to assess specific variables (Creswell and Plano Clark 2007). Researchers present their findings as numbers, percentages and means in charts and graphs (McGivern 2006). Table 4.3 displays the differences between qualitative and quantitative research.

Although researchers have traditionally chosen between qualitative and quantitative methods, they now consider mixed methods research to be a viable option. Doyle et al. (2009) suggest that this is a response to the limitations experienced using methods individually and the greater acceptance of mixed methods research by the academic community. Tashakkori and Creswell (2007 p4) define mixed methods research as:

> *research in which an investigator collects and analyses data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or program of inquiry.*

The rationale for using a combination of data sources is that mixed methods expose different views and multiple stakeholder perceptions and experiences of clinical trials. As Bryman et al. (2008) suggests, each method of data collection represented in the evaluation of clinical trials becomes '*an important piece of a jigsaw'* (p264). Greene, Caracelli and Graham (1989) present five possible advantages of using mixed methods research: (1) initiation—discovering fresh perspectives through paradoxes and apparent contradictions; (2) triangulation—testing the convergence or validity of results; (3) complementarity—elaboration, enhancement, illustration and clarification of results; (4) development—using the results from the first methods to inform, design and implement the second method; and (5) expansion—extending the breadth or scope of the project. The researcher considers initiation, triangulation, complementarity and expansion are important as a means of contributing breadth and depth to this study.

TABLE 4-3 ELEMENTS OF QUALITATIVE AND QUANTITATIVE RESEARCH (SOURCE: CRESWELL AND PLANO CLARK 2007 P29)

Elements of qualitative research tend towards	Process of research	Elements of quantitative research tend towards
Understand meaning individuals give to phenomenon inductively	Intent of the research	Test a theory deductively to support or refute it
Minor role Justifies problem	How literature is used	Major role Justifies problem Identifies question or hypotheses
Ask open-ended questions Understand the complexities of a single idea or phenomenon	How intent is focused	Ask closed-ended questions Test specific variables that form hypotheses or questions
Words and images From a few participants at a few sites Studying participants at their location	How data are collected	Numbers From many participants at many sites Giving instruments to participants
Text or image analysis Themes Larger patterns or generalisations	How data are analysed	Numerical statistical analysis Rejecting Hypotheses or determining effect sizes
Identifies personal stance Report bias	Role of the researcher	Remains in background Takes steps to remove bias
Using validity procedures that rely on the participants the researcher or the reader	How data are validated	Using validity procedures based on external standards, such as judges, past research and statistics

Creswell and Plano Clark (2007) identify four situations in which mixed methods research should be the preferred research methodology. These include when: (1) either a quantitative or

qualitative study is inadequate in itself to address the research problem; (2) there is a need to enhance a study with an additional source of data, i.e. a quantitative study enhances a qualitative study or a qualitative study enhances a quantitative study; (3) there is a need to explain the quantitative results; and (4) there is a need to explore qualitatively before undertaking a quantitative study. Although the researcher initially considered a single approach for this study, she rejected this because neither a qualitative nor a quantitative methodology used individually is likely to answer the research questions. The complex nature of the health industry may explain the increasing tendency to use mixed methods research in health management research. Freyens (2008 p830) describes the health industry thus:

> *This industry has long-faced intrinsic input problems (skill shortages and high technology cost of some services) and demand problems (expenditure is demand driven and therefore hard to control). Outputs are hard to measure (good health outcomes appear less related to health services than income) and consist of a large array of medical and health services, hospital and nursing care, subsidised pharmaceutical products, health research, health insurance etc.*

Twinn (2003) suggests that mixed methods research addresses the complex questions frequently asked in this industry. With complex intertwining issues surrounding the benefits and costs to several stakeholder groups (trial participants, caregivers, researchers, staff, pharmaceutical companies and government decision makers), mixed methods research is a practical choice for this study. Giddings (2006) gives a second reason for the increased use of mixed methods research in the health industry. She asserts mixed methods research is attracting more research funding, as funding bodies are increasingly encouraging collaborative research projects with nursing, medical and paramedical professionals using a variety of methods. With medicine traditionally associated with quantitative research and nursing with qualitative research, the interdisciplinary mixed methods research team can utilise the strengths of mixed methods research (Doyle et al. 2009).

Mixed methods research also meets the needs of multiple and diverse stakeholders for a project including those who need hard data for their decision-making and those who wish to understand better the feelings of the participants. As Greene (2005 p209) observes '*A mixed method approach offers greater possibilities than a single method approach for responding to decision-makers agenda, as well as to the interests of other legitimate stakeholders*'. This quality was

influential in the choice of design for the current study, as although politicians require quantitative information to guide their allocation of health care resources other stakeholders including patient groups may not place the same importance on financial metrics. Mixed methods research has emerged as the appropriate methodology for the current study.

The current study keeps the qualitative and quantitative data separate to realise the strengths of each approach (Teddlie and Tashakkori 2009). Brewer and Hunter (2006) suggest qualitative and quantitative comparison compromises the strengths of these methods. This is consistent with the view held by Sale, Lohfeld and Brazil (2002) who suggest that when qualitative and quantitative methods study different phenomena these methods *cannot be combined for cross-validation or triangulation purposes. However, they can be combined for complementary purposes* (Sale, *et al* 2002, p43).

As data relating to many aspects of the study can be obtained via only one of the available research methods, the researcher adopts the view that quantitative and qualitative methods can be combined in the current study only for complementary purposes. While the data do not support triangulation between the qualitative and quantitative methods, the qualitative analysis complements the quantitative analysis. A pragmatic worldview suggests that researchers present the results in a way that best suits the situation and intended audience. With this in mind, this thesis reports the economic outcomes and the multiple stakeholder perceptions strands separately in chapters 5 and 6. Chapter 7 reveals the power of a complementary treatment of these approaches.

Mixed methods refer to both a methodology and a research design. Creswell and Plano Clark (2007 p. 5) explain these dual roles by defining mixed methods as follows:

> *Mixed methods research is a research design with philosophical assumptions as well as methods of inquiry. As a methodology, it involves philosophical assumptions that guide the direction of the collection and analysis of data and the mixture of qualitative and quantitative data in a single study or series of studies. Its central premise is that the use of quantitative and qualitative approaches in combination provides a better understanding of research problems that either approach alone.*

The next step in the research process is the research design.

RESEARCH DESIGN

A research design provides a strategy or blueprint specifying the methods and procedures used for collecting and analysing data (Carter and Little, 2009). The idea of mixing research methods is relatively recent, though the number of designs incorporating mixed methods research is growing (see for example; Cresswell 2003, DePoy and Gitlin 1994, Morgan 1997). There are three key decisions a researcher makes when designing a mixed methods study (Creswell and Plano Clark 2007). The first decision is the timing decision, which is based on the timing of the stages, and whether qualitative and quantitative approaches are to be used concurrently or sequentially (Creswell and Plano Clark 2007). Following a review of 48 mixed methods research studies, O'Cathain et al. (2007) found that within the field of health research 60 percent of studies are sequential. Nevertheless, this study adopted a concurrent design to take advantage of the complementary nature of the qualitative and quantitative findings. Using a concurrent design, the benefits and costs identified in the economic strand are further illuminated in the multiple stakeholder perceptions strand and vice versa. This two-way interaction is not possible in a sequential design, which completes one strand before beginning the other.

The second decision in mixed methods research design is the weighting decision, which focuses on the status of qualitative versus quantitative methods. How the weighting is determined and what the weightings are has strong design and resource implications. The weighting influences the complexity and sophistication of the procedure used for each method (Creswell and Plano Clark 2007). If both methods have equal weighting, the study requires more resources (Creswell 2003). There are many interpretations available on when, where and how a researcher should weight quantitative and qualitative strands. Possibilities include weighting strands according to their division in the research design, the time taken to undertake each strand, the quantity of data generated by each strand or the relative importance given to each type of result (Hall and Howard 2008). The interpretation adopted for this study is the priority or relative importance given to each strand in answering the research questions (Morgan 1998, Cresswell and Plano Clark 2007). The current study gives equal priority to the two strands as the researcher regards both the qualitative (stakeholder perceptions) and quantitative (economic outcomes) strands equally important in addressing the research questions. Each strand delivers dimensions to the

analysis that are not apparent from the other. The third decision is the mixing decision, which determines how the quantitative and qualitative sets of data will be explicitly related.

Principles or values can guide the choice of research design. Three key principles developed by Hall and Howard (2008) influence the choice of design in this study. These principles are: (1) that qualitative and quantitative methods interact so that their combined effect is greater than the sum of their individual effects. 2) that equal value is placed on the outcomes of the qualitative and the quantitative methods. When applied to the current study this means that neither approach is valued more highly than the other, (3) that paradigmatic differences are protected while choosing the methods that provide the greatest opportunities within the research design. There are some research perspectives in this current study that are better suited to a quantitative approach (research perspectives 1-3) while perspectives 4-10 are best answered using a quantitative approach. As outlined in chapter 1 the current study considers the benefits and costs from several different perspectives. The study first quantifies the benefits and costs from the perspective of:

1. the Centre for Clinical Research and Effective Practice (CCRep);
2. Counties Manukau District Health Board (CMDHB);
3. New Zealand society.

It next establishes the benefits and costs of sponsored clinical trials as perceived by:

1. trial participants;
2. trial participants' family member and caregivers;
3. Counties Manukau District Health Board staff;
4. researchers;
5. the Counties Manukau community;
6. government, government bodies and politicians; and
7. members of the pharmaceutical industry.

Teddlie and Tashakkori, (2009) develop a typology of mixed methods designs that identifies five families of multistrand mixed methods designs: (1) parallel, (2) sequential (3) conversion (4) multilevel and (5) fully integrated. Multistrand mixed methods designs have more than one strand where each strand includes three stages – the conceptualisation stage, the experimental stage and the inferential stage. In parallel mixed methods multistrand designs the researcher conducts quantitative and qualitative strands independently in a parallel manner. Data are

collected and analysed concurrently. Meta inferences are drawn at the end. Meta inferences are conclusions drawn from the integration of the independent strands and can take several forms (Teddlie and Tashakkori, 2009). The sequential mixed methods multistrand design occurs when one strand follows a second strand in a chronological order. One example of this is where qualitative techniques are added to a quantitative study such as the adding of open-ended questions at the end of a survey. In the conversion model, data are collected concurrently before being transformed either by quantifying the qualitative data or by qualifying the quantitative results. The multi-level model is when the focus of the study is on a system and different methods are used to address the different levels within the system. Finally, the mixed design is a multi-strand parallel design in which mixing of economic and multiple stakeholder perceptions strands occur throughout the study in an iterative manner.

The design most suited to this study is a simultaneous parallel three-strand mixed methods design. Figure 4.2 shows how the three strands contribute to the final analysis: (1) a health outcomes strand involving a retrospective cohort study of participants in sponsored clinical trials, (2) a multiple stakeholder perceptions strand assesses stakeholder perceptions of two clinical trials being performed at CMDHB and (3) an economic outcomes strand evaluates the benefits and costs of clinical trials.

In the multiple stakeholder perceptions strand, the current study uses qualitative methods to explore the benefits and costs perceived by stakeholders. In the economic outcomes strand, it uses quantitative methods to estimate the benefits and costs of clinical trials. The reason for collecting both quantitative and qualitative data is to bring together the strengths of both forms of research to compare, validate and corroborate results. The current study applies 'parallel mixed data analysis' (Teddlie and Tashakkori 2009) in the form of two separate and independent processes to the data analysis. The researcher applies (1) a qualitative descriptive analysis coupled with a phenomenographical analysis for the multiple stakeholder perceptions strand and (2) a quantitative analysis relying on various data sources for the economic outcomes strand to produce a strong evaluation of clinical trials. The economic outcomes strand and the multiple stakeholder perceptions strand are complementary.

Adopting this design, the current study collects the data in strands in parallel (see figure 4.1). The clinical trials connect the strands at the top of the diagram. The strands progress through parallel data collection and data analysis phases to produce independent outcomes. The

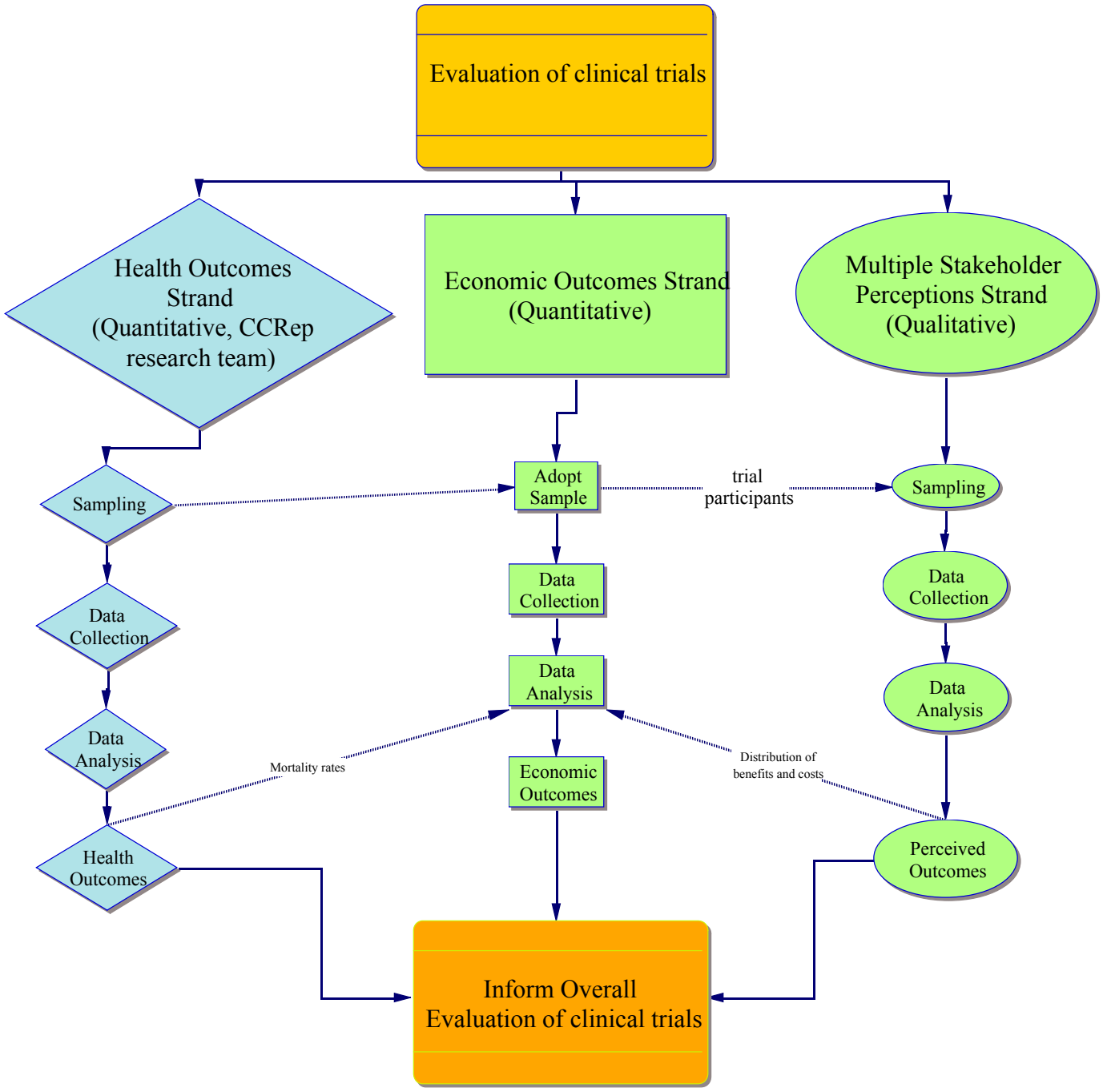
economic outcomes strand connects with the health outcomes study at two points: (1) in the sample selection where both the economic outcomes stand also the health outcomes study use the same cohort matched controls and provides a sample for the multiple stakeholder perceptions strand, and (2) during data analysis when the study uses the results from the health outcomes strand as a basis for costing treatments in the economic outcomes strand. The stakeholder perception strand feeds into the economic outcomes strand towards the end of the analysis when the distribution of the benefits and costs is determined. The study concludes by considering the three sets of outcomes for a collaborative evaluation of sponsored clinical trials at a publicly funded New Zealand hospital.

The research process begins with the identification of a broad research problem. The identification of the paradigm and the development of the methodology occur next as described previously in this section. Using a complementary paradigm perspective, the analyses needed to meet the research objectives are determined. This influences the development of the study design and method selection, which provides a guide for the interactive, circular process of data collection, data analysis, and design review that follows until saturation is reached and no new information emerges (Lincoln and Gubra 1985). The data using inductive and/or deductive reasoning are analysed. A qualitative multiple stakeholder perceptions strand gathers information from the participant groups. Conclusions are reached after analysing the benefits and costs revealed from comparing the quantitative and qualitative data. These data inform the final discussion and conclusions.

RESEARCH METHODS

Research methods include the research activities of: (1) sampling, (2) data collection, (3) data management, (4) data analysis, and (5) reporting (Carter and Little 2007). Mixed methods research uses a combination of qualitative and quantitative research methods. This may mean

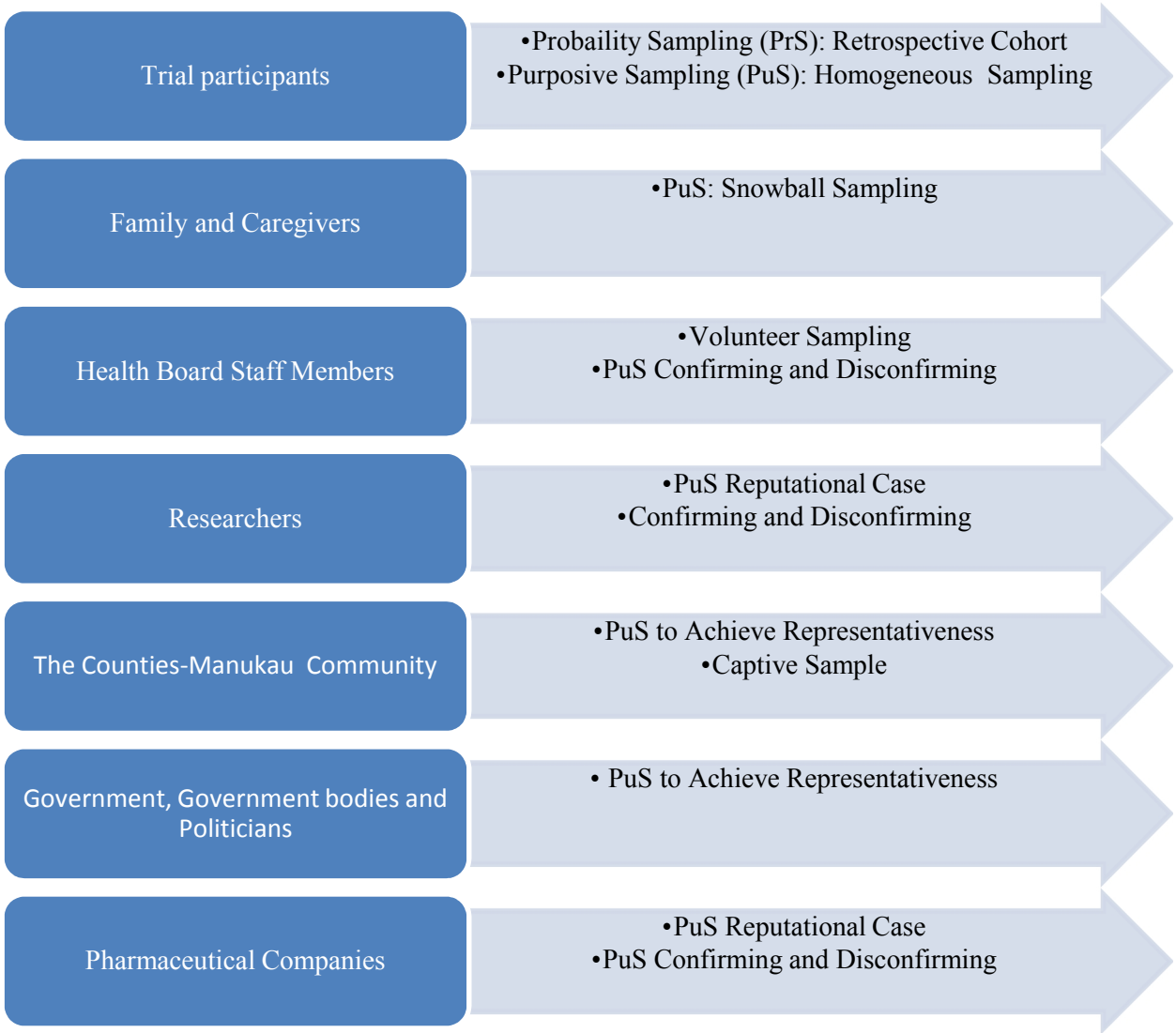
FIGURE 4-2 RESEARCH DESIGN (SOURCE: MURPHY AND MAGUIRE 2011).



one or several methods representing each research approach. In well-designed mixed methods research the specific research questions, the data collection and the ways in which evidence is interpreted complement one another. In addition, as each method has its own limitations or

imperfections these are compensated for by using a mixture of methods (Brewer and Hunter 1989).

FIGURE 4-3 SAMPLING TECHNIQUES USED AS CLASSIFIED BY TEDDLIE AND TASHAKKORI (2009).



Sampling is a process for selecting elements for analysis (for example participants, groups, artefacts, settings) which maximise a researcher's ability to answer research questions (Tashakkori and Teddlie, 2003. The current study applies a pragmatic approach to developing the sampling strategy for the parallel design. It identifies possible sampling approaches from the

typology of sampling techniques developed by Teddlie and Tashakkori (2009). Figure 4.3 shows the sampling techniques that vary across stakeholders in this study.

The strands progress through parallel data collection and data analysis phases to produce independent outcomes. The researcher applies 'parallel mixed data analysis' (Teddlie and Tashakkori, 2009), two separate and independent processes, to the data analysis. The researcher uses:

(1) a qualitative descriptive analysis coupled with a phenomenographical analysis for the multiple stakeholder perceptions strand; and

(2) a quantitative analysis relying on various data sources for the economic outcomes strand.

Collectively the results provide complementary evidence and contribute to a comprehensive understanding of the outcomes of clinical trials in New Zealand. CCRep conducts the quantitative health outcomes strand of the study separately and it is not part of this PhD research. For this reason, the researcher refers to the health outcome quantitative outcomes strand only briefly here. The next focus is on the economic strand and then the multiple stakeholder perceptions strands of the current study.

ECONOMIC OUTCOMES STRAND

Micro costing is a valuation method in health economics, where the unit of analysis is the individual or individual service (Drummond et al. 2000). The method measures costs and benefits of a service as accurately as possible, by including all fixed and variable costs of care at local prices. The micro-costing approach provides the most precise estimate of health care costs used in health care evaluation (Drummond et al. 2000). The current study uses micro costing to assess health care costs by establishing health utilisation in the participant and matched control group and then multiplying these by unit costs. This section begins with a discussion on approaches to economic evaluation and justifies the selection of a BCA as the most appropriate for this study. It then details the approach of BCA.

ECONOMIC EVALUATION

Gold, Siegel, Russell and Weinstein (1996) distinguish economic evaluation from other forms of evaluation using two key features: (1) it consists of both costs and consequences and (2) it

involves a comparison of alternatives. Economic evaluation focuses on marginal costs and marginal utilities. The marginal cost of an additional unit of output is the cost of the additional input needed to produce that output (Gold et al. 1996). The marginal benefit of a treatment is the additional benefit from one additional unit of treatment. This is important when measuring the value of one programme against another programme when budgets are tight. Mooney (2003 p13) state:

> *If no budget constraint exists then a programme should be expanded or contracted to a point where marginal benefit equals marginal cost; if there is a budget constraint, then all programmes should operate at a level whereby the ratio of marginal benefit to marginal cost is the same for all.*

Several forms of economic evaluation are considered for this study including: cost minimisation analysis (CMA), cost consequence analysis (CCA), cost effectiveness analysis (CEA), cost utility analysis (CUA) and benefit cost analysis (BCA). BCA has a long history as a method of economic evaluation. A 1772 letter written by Benjamin Franklin is the earliest recorded use of BCA In the letter he explains a problem solving method which he calls 'Moral or Prudential Algebra' (Gramlich 1981 p1).

> *Divide a sheet of paper in half, and make an exhaustive list of pros and cons. Then, over a couple days, weigh the pros and cons, and when pros and cons seem of equal weight, strike them both out. Use this method even if one con is equal to three cons*

The balance, suggests Franklin, is the best answer. This approach to problem solving has many similarities with current approaches to BCA in that it analyses pros (benefits) and cons (costs), assigns weights (a dollar value), and then determines whether or not the benefits outweigh the costs (Gramlich 1981). The 1936 US Flood Control Act, which required all new United States Army Corps of Engineers projects to have a BCA, provides the basis to current practice (Dobes 2007). The current study uses a BCA for the economic analysis because a BCA is able to take into account the widest range of benefits and costs (Boardman et al. 2006).

DATA COLLECTION

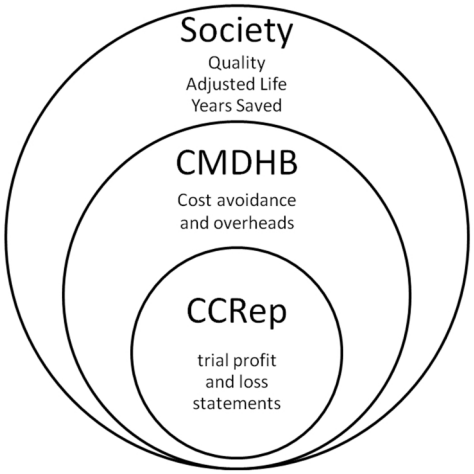
The economic strand of the project investigates two clinical trials over an eight-year period including pre-trial, trial and post-trial stages. As indicated in chapter 3 while this time period is

greater than the one year time period recommended by Fireman et al. (2000), it is selected for three reasons (1) it allows comparisons between trial stages, (2) it allows the study to benefit from the health outcomes study conducted by CCRep, using the same time period and (3) as this study involves a retrospective cohort design collecting data for the full eight year period involves little additional effort.

SPREADSHEET-BASED MULTIPLE ACCOUNT APPROACH

Benefit cost analysis (BCA) has little or no meaning without specifying a focal stakeholder that receives the benefit or bears the cost. While CCRep clearly has a central interest, the current study involves a range of stakeholders. This study accordingly presents the analysis for the economic outcomes from three perspectives by adapting a spreadsheet-based multiple account approach (Campbell and Brown, 2003). The three sections of the spreadsheet reflect BCAs from different but related perspectives, namely: (1) the CCRep research unit (micro-level), (2) the CMDHB (meso-level) and (3) New Zealand society (macro-level).

FIGURE 4-4 THE THREE PERSPECTIVES USED IN THE BENEFIT COST ANALYSIS



Data for the CCRep perspective are drawn from profit and loss statements relating to the two trials (see figure 4.4). The analysis from the CMDHB perspective considers the CMDHB budget impacts from involvement in clinical trials. It encapsulates the CCRep revenues and costs as well as CMDHB costs, cost savings and cost avoidance from pharmaceutical and laboratory subsidies,

patient treatment programmes, and indirect costs. The societal perspective builds on the CMDHB perspective and takes into account the changes in health status and value of lives saved because of the clinical trials. Using data showing the differences between mortality levels in case and control groups reported in the health outcomes strand, the researcher calculates quality adjusted life years (QALY) as a measure of societal benefits from clinical trials. This study provides two scenarios for the BCA from the view of society, the first using a plausible but high value for QALY and second using a plausible but low QALY value. Table 4.5 provides a summary of the data sources for this strand.

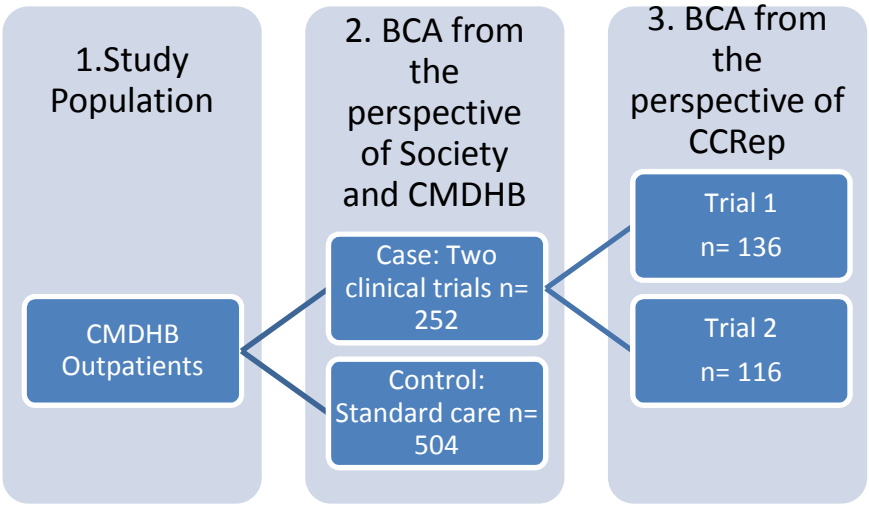
TABLE 4-4 DATA SOURCES FOR THE ECONOMIC STRAND OF THE STUDY (SOURCE MURPHY AND MAGUIRE 2011).

Data Type	Details	Source
BCA CCRep		
Revenue	Revenue from trial profit and loss accounts	CCRep: Profit and Loss Statement
Direct costs: Clinical Trial	Trial profit and loss accounts	CCRep: Profit and Loss Statement
BCA: CMDHB		
Overhead costs		CMDHB
Hospital Outpatient costs	Chronic Care Management Programme (CCM) costs	CMDHB: CCM data
Pharmaceutical costs	Pharmaceuticals prescribed	Pharmaceutical Schedule (PHARMAC)
Laboratory costs	Costs of outpatient laboratory and diagnostic tests	Ministry of Health Data Bank: LABS
BCA: New Zealand society		
Mortality	Health Outcomes for trial participants and standardised treatment	Health Outcome study (CCRep)
Quality of life	Utility rating in the form of a single number representing the net aggregate impact of physical, emotional and social functioning on quality of life	EQ-5D Tariff Access Economics value of statistical life PHARMAC investment in new health technologies

RESEARCH DESIGN

The research design for the economic strand builds on the health outcomes strand that involves a cohort study of changes in participants' health status and mortality rates. Links are made at two points: (1) in the sample selection (the economic outcomes strand and the health outcomes strand use the same cohort matched controls) and (2) during data analysis when the changes in mortality levels identified in the health outcomes strand are used to proportion costs in the economic outcomes strand (see figure 4.2 in the previous section).

FIGURE 4-5 STUDY GROUPS FOR THE ECONOMIC ANALYSIS (SOURCE; MURPHY AND MAGUIRE 2011).



Detailed analysis of the health outcomes strand is outside the scope of this paper because the CCRep research team conducted it and will report on it (forthcoming). A key reason for using a retrospective cohort design is the opportunity to link this study with the concurrent study on health outcomes, which allows access to data that would have been otherwise difficult and expensive to obtain.

Figure 4.5 illustrates the selection of study groups for the three perspectives. First the study population (CMDHB outpatients) shown in box 1 is divided into two groups (box 2). The case group comprises those enrolled in a clinical trial and the control group comprises those who receive the standard outpatient care. The researcher compares the benefits and costs for the case and control groups from the perspectives of CMDHB and New Zealand society respectively.

Next, it divides the case group into the two separate trials (box 3). It compares the two trials when it investigates the benefits and costs from the perspective of CCRep.

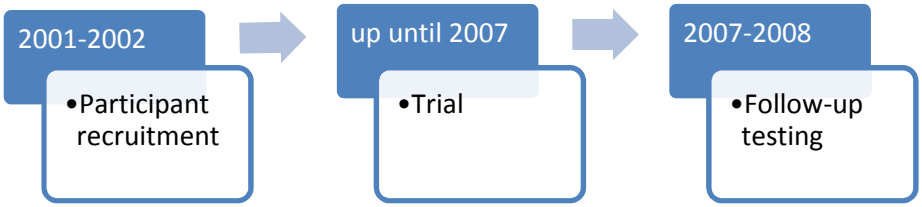
PROCEDURES

The current study begins the benefit cost analysis from the perspective of CCRep using CCRep archived profit and loss statements relating to the two contributing clinical trials to construct a comparative benefit cost analysis that values all inputs and outputs at current market prices (tables 5.1 and 5.2 in the next chapter). As discussed in chapter 2 the costing units used in financial data can influence the accuracy of financial accounts. Table 5.3 details of the costing units the study adopts. CCRep supplies the profit and loss statements. The accuracy cannot be verified, however as the contents are not under the researcher's control. The researcher uses this data, as it is the best data available. The sponsors of clinical trials consider cost data commercially sensitive information and therefore can this information can be difficult to access. Trial 1 has 136 participants. Trial 2 has 116 participants. As each clinical trial has a different number of participants, the researcher compares average cost and revenue per participant. The researcher analyses the two clinical trials by taking into account the benefits and costs *that accrue to the enterprise itself and affect its profitability* (Campbell and Brown 2003 p 62). Therefore, at this point the researcher does not take into account items such as indirect costs funded through CMDHB. The researcher investigates the two clinical trials over an eight-year period including recruitment, trial and follow-up testing stages (see Figure 4.6).

The CMDHB, analysis identifies the types and quantities of resources utilised by case and control groups and assesses whether the resources utilised differs between them. Cases are 252 men and women at high risk of cardiovascular events, aged under fifty-five years of age. They were enrolled in two long-term Phase III randomised, controlled clinical trials designed to assess preventative medication for patients at risk of serious cardiovascular events. The current study analyses data from the case and control groups investigated in the health outcomes study. CCRep identified the control group by age, gender, and ethnicity-matched patients from their decision-support records (Casemix™). The patients were inpatients or attended outpatient clinics at the

research site at the time of the trials[2]. As the two clinical trials have the same recruitment criteria and the study requires a larger sample for a full mega analysis, they are combined for the analysis from the perspective of CMDHB. The case and control groups are consistent with those used in the health outcomes strand of the wider study.

FIGURE 4-6 THE CLINICAL TRIAL PROCESS SHOWING RECRUITMENT, TRIAL AND FOLLOW-UP PERIODS.



The researcher identifies several types of resources for the benefit cost analysis from the perspective of the CMDHB. The researcher uses the ingredients approach to collect data. The ingredients approach is a detailed micro-costing approach, often referred to as bottom-up costing, in which the resource data are collected from the first principles in a study. The resource use is quantified directly rather than relying upon secondary sources of data. This is the most detailed and potentially accurate method to quantify resources. It allows the validation of the assumptions used and the ability to change parameters easily if required. Separate evaluations for case and control groups are conducted (Baltussen, Adam, Tan Torres, Hutubessy, Acharya and Evans 2002).

The BCA from the perspective of New Zealand society includes the benefits and costs identified earlier from the perspective of CMDHB and CCRep as well as the benefits from reduced mortality levels. Using data showing the differences between mortality levels in case and control groups reported in the health outcomes strand, the researcher calculates QALY as a measure of societal benefits from clinical trials. The researcher converts the life years saved to QALY by

[2] The two groups of 252 patients are selected for the health study to provide at least 80% power (at the 5% significance level) to detect an 8.6% difference (two-tailed) in event rate between groups based on a composite endpoint event rate of 16.8% in the placebo-treated group in the study over a mean 4.3 years of follow-up (i.e. 16.8% ± 8.6%). A mixed models approach to repeated measures is employed to test this hypothesis. This results in a modification to increase the ratio of control to increase the power (the ratio is 2:1).

applying a utility weighting to take account of disability levels and then multiply this by the value of a statistical life year (SLY). The researcher takes a society view when valuing QALY.

DISCOUNT RATE AND SENSITIVITY ANALYSIS

The researcher discounts benefits and costs that occur at different time periods in the analysis. No one method of determining the discount rate has universal acceptance (PHARMAC 2007). The International Society of Pharmacoeconomics and Outcomes Research (ISPOR) suggests that a discount rate of either 3% or 5% followed by a sensitivity analysis between 0% and 10% (Dix Smith et al. 2003). These internationally based recommendations may not be appropriate for the New Zealand environment. PHARMAC (2007 p52) suggest three reasons that it may be erroneous to use an international discount rate within New Zealand:

1. New Zealand's economic performance is not identical to that of other economies hence the use of an international discount rate may not reflect societal or individual preferences in New Zealand.
2. Economic analyses cannot be directly transferred or compared between countries.
3. The risk-free bond rate and resources available in New Zealand are not identical to that in other countries

Access Economics (2008b) use a discount rate of 3.65% for their New Zealand based study on the economic impact of dementia. They base this rate on long-term nominal bond rates, consumer price index target inflation outcomes and productivity growth. Although Access Economics use a sound methodology for establishing their discount rate for consistency across studies, the researcher adopts the more commonly used PHARMAC recommendation to discount all costs and benefits using the 5-year average real risk-free long-term government bond rate of 3.5%. (PHARMAC 2007 p53)

> *PHARMAC considers that the social rate of time preference is the most relevant approach for PHARMAC to use when determining the discount rate as it reflects society preferences. This requires the use of the long-term government bond rate*.

This rate is agreed by Boardman et al. (2006) who recommend that projects of fewer than 50 years should use a discount rate of 3.5 percent which they believe most accurately reflects the shadow price of capital. The shadow price of capital is defined as '*the loss to society that occurs*

when a dollar that would otherwise have gone to private investment is displaced' (PHARMAC 2007 p52).

Pizzini (2006) highlights the value of data that provide sufficient detail and flexibility to allow costs to be analysed for a variety of purposes. However, the benefits of such a system must be weighed against the costs associated with collecting the data. Data that are routinely available within the New Zealand health sector can present accuracy and validity problems. PHARMAC 2005 p12 issues this warning about clinical evidence:

> *In general there are few timely data available about the types of patients, disease/disability rates and pharmaceutical indications conditions treated in primary care, particularly when subdividing ethnicity by disease/indications. Mortality data are less timely than hospitalisations data and give less precise estimates of risk (given smaller numbers of deaths). Maori death rates have in past decades been substantially under-represented due to ethnicity miscoding. Causes of death described on death certificates can be inaccurate. Routinely collected hospitalisations data are less accurate than mortality data, with historically over one-quarter of discharge diagnosis being incorrectly coded.*

Notwithstanding these flaws, PHARMAC (2007) advises against using overseas cost data due to possible differences in clinical practice, pricing structures and opportunities to redeploy resources. Determining benefits and costs can be difficult and choices must be made in their definition and measurement (Oakes, Considine and Gould 1994). Uncertainty occurs when the true value of a parameter is not known and as *no data are entirely free of error,* uncertainty must be accounted for in health outcomes research (Muennig 2007 p 37). The researcher therefore seeks New Zealand cost data for the evaluation and use sensitivity analysis to account for the uncertainty in that data.

TABLE 4-5 SENSITIVITY ANALYSIS USED FOR EACH PERSPECTIVE IN THE ECONOMIC OUTCOMES STRAND.

BCA Perspective	**Sensitivity Analysis Used**	**Focus**
CCRep	One way sensitivity analysis	Discount rate
CMDHB	One way sensitivity analysis	Savings from cost avoidance
		Discount rate
Society	Extreme scenario sensitivity analysis	Value of QALY
	One way sensitivity analysis	Discount rate

While it is generally agreed that sensitivity analysis can be used to investigate the impact of uncertainty and risk in an economic evaluation, there are few agreed guidelines on how to conduct or interpret sensitivity analyses in health economic evaluations (Dix Smith et al. 2003). In addition, as every assumption in a BCA can be varied, there are practical limits to the amount of sensitivity analysis that is feasible (Boardman et al. 2006). The current study considers the uncertainty and risk of the data used for the micro, meso and macro perspective analysis. As each perspective uses different sources of data and the risk and uncertainty of the data varies across sources. The researcher uses a different approach to sensitivity analysis for each perspective of the BCA (Table: 5.4). The data from the perspective of CCRep has the least uncertainty and risk as it is collected close to the source and is based on a standardised trial protocol. The researcher therefore conducts a one-way sensitivity analysis on the net present value (NPV) of the clinical trial surplus. Performing a sensitivity analysis by varying only the discount rate is a commonly used method of taking risk into account (Campbell and Brown2003). This in effect allows a risk premium to be added to the discount rate rather than assessing the sensitivity of each individual assumption as Campbell and Brown (2003 p196) explain:

> *Providing the decision maker with NPV's for a given project over a range of discount rates provides the information necessary to assess the significance of applying a risk premium, and deciding whether a project is marginal or not.*

The current study uses a range of discount rates in performing the sensitivity analysis, namely those that PHARMAC recommends 0%, 5% and 10%. Rates of 0%, 5%, and 10% enable comparison with analyses undertaken in other countries (5% and 10%), and the impact of the discount rate (0%). In the current study there are accuracy risks in the data on savings from cost avoidance in the CMDHB BCA. A one-way sensitivity analysis is conducted as a means of dealing with the study's uncertainties (Dix Smith et al. 2003). A one-way sensitivity analysis examines the impact of one variable in the study by varying it across a range of plausible values while holding all other variables constant at their most plausible level (Boardman et al. 2006). As a response to the uncertainty, surrounding the accuracy of Ministry of Health (MOH) data the first variable examined in the one way sensitivity analysis is the savings from cost avoidance. The researcher initially varies the value for cost avoidances by plus or minus 5 percent. The researcher further increases the value of savings by cost avoidance to plus or minus 15 percent

and assesses the impact this has on the outcome of the BCA. The researcher then conducts a one way sensitivity analysis is conducted on the NPV as outlined above.

MULTIPLE STAKEHOLDER PERCEPTIONS STRAND

As identified in chapter 2, stakeholder theory provides justification for the choice of stakeholders in the multiple stakeholder perceptions strand of the current study. Collier (2008) identifies the

FIGURE 4-7 COMPARISOM BETWEEN STAKEHOLDERS IDENTIFIED BY COLLIER (2008) AND THOSE SELECTED FOR CURRENT STUDY.

Stakeholder groups identified by Collier (2008)	**Stakeholder groups multiple stakeholder perceptions strand of current study**
Service recipients	Trial participants
	Family and caregivers
Employees	Health board staff members
	Researchers
Tax payers	Counties-Manukau community
Government	Government, government bodies and politicians
Suppliers	Pharmaceutical industry
Lenders	

stakeholders in this quasi government sector as consisting of service recipients, employees, taxpayers, government, suppliers and, lenders. The current study uses this as a base and makes additions and deletions to accommodate the unique environment of sponsored clinical trials. The current study subdivides Collier's stakeholder group 'service recipients' to include 'trial participants' and 'family and caregivers'. 'Family and caregivers' are stakeholders because they *'place something of value 'at risk'; that is, their own welfare is directly 'affected by the fate of the enterprise'* Kochan and Rubenstein (2000 p373). The 'something' they place at risk is their family member or person they care for. The current study also subdivides Collier's stakeholder category 'employees' to include 'researchers' and 'health board staff members'. These groups may have different perceptions of clinical trials due to their differing involvement. The current study narrows Collier's stakeholder group 'taxpayers' to include only members of the 'Counties-

Manukau community' who living near-by are the most effected taxpayers. The current study further divides Colliers stakeholder group 'government' to include 'government, government bodies and politicians'. This wider group takes into account the importance of government bodies such as Medsafe and PHARMAC to the study and the multiple levels of affected politicians namely elected members of the health board, local and central governments. Finally the current study selects the 'pharmaceutical industry' to represent Collier's stakeholder group 'suppliers' as they supply the sponsorship needed for the trial. There are no lenders in the current study so this group is not included.

The qualitative methods include focus groups, interviews, posted and on-line surveys. The researcher considers different methods for each participant group to allow for communicative preferences. Hoffman (2009 p10) asserts that communicative preferences explain why research methods that are optimal for some participants, shut down meaningful participation for others and suggests that research methods should be selected according to the communication preference of the participant, not the researcher.

> *While there are important advantages and disadvantages (for the researcher) associated with the use of different types of research methods within the same study, I will point out that if the object of the game is to stimulate participation in the research; using a variety of methods that corresponds to the communicative preferences of our potential participants, may be a better starting point than our own communicative preferences*.

Following consultation at the design stage of this study, some participants indicate a strong preference for one method over another. In particular, the pharmaceutical company representatives cite busy schedules as grounds for not participating in focus groups but indicate a willingness to participate in interviews. This is also the case with most politicians. A researcher informant is happy to complete a survey but again because of time constraints declines to be part of an interview or focus group.

DATA COLLECTION

The researcher asks the same questions of each stakeholder group irrespective of the data collection method used to facilitate a comparison of their responses (see Table 4.6). This uncovers differing perceptions; for example, health board staff members feel that trial

participants gain the most benefit from the new treatment drugs being offered whereas trial participants identify the additional care and attention as the greatest benefit.

SAMPLING METHODS

For the multiple stakeholder perceptions strand the researcher uses purposive sampling methods to recruit informants who have experienced clinical trials and/or are members of the identified stakeholder groups. Hoffman (2009 p7) explains purposive selection:

> *Purposive selection means that research settings, data from these settings and research participants are located with reference to theory that indicates the selection is likely to address or lead to data that can answer research questions. Using theoretical concepts to guide the selection of data from the beginning—at the design stage of research—is the first step to interpretive data analysis designed to generate analytical generalizations — to theory*.

Large samples are not needed to compile the rich data sets as each individual informant can generate multiple ideas (Starks and Brown Trinidad 2007). The intention was to continue to collect data until the analysis reaches saturation – 'the point at which no new information or themes are observed in the data' (Guest, Bunce and Johnson 2006 p59). However, the statement of this intention was insufficient to gain ethics approval. The researcher was asked to provide more specific data on the proposed sample size.

TABLE 4-6 FOCUS GROUP, INTERVIEW AND SURVEY QUESTIONS

1. How does the international community benefit from clinical drug trials?
2. What are the risks, tradeoffs, disadvantages or costs to the international community in conducting clinical drug trials?
3. How do pharmaceutical companies benefit from clinical drug trials?
4. What are the risks, tradeoffs, disadvantages or costs to pharmaceutical companies in conducting clinical drug trials?
5. How do other New Zealanders benefit from clinical drug trials performed in Counties Manukau?
6. What are the tradeoffs, disadvantages or costs to other New Zealanders in Counties

Manukau conducting clinical drug trials?

7. How does Counties Manukau District Health Board benefit from sponsoring clinical drug trials?
8. How do staff benefit from clinical drug trials performed at Middlemore Hospital?
9. How do staff benefit from clinical drug trials performed at Middlemore Hospital?
10. What are the tradeoffs, disadvantages or costs to Middlemore Hospital staff in conducting clinical drug trials?
11. How do participants benefit from being part of a clinical drug trial?
12. What are the tradeoffs, disadvantages or costs to participants in being involved in a clinical drug trial?
13. How do the care givers of trial participants benefit from clinical drug trials?
14. What are the tradeoffs, disadvantages or costs to the care givers of trial participants in being involved in a clinical drug trial?
15. What are the tradeoffs, disadvantages or costs to Counties Manukau District Health Board in conducting clinical drug trials?

Morse (2000) identifies factors to consider when determining sample size for qualitative research including the (1) scope of the study, (2) quality of the data, (3) nature of the topic, (4) study design and (5) use of shadowed data. Shadowed data occur when informants in addition to talking about their own experience, discuss the experience of others (Morse 2000).Using these criteria the researcher identifies the broad nature of the multiple stakeholder perceptions strand questions as a factor that suggests the researcher should consider a large sample size. Countering this and guiding the decision to keep the sample size small is the clear nature of the topic, the willingness of the informants to share their experiences and provide quality data, the collective unit of analysis in the study design and the use of shadowed data. Morse, (2000 p4) explains the value of shadowed data:

> *it provides the investigator with some idea of the range of experiences and the domain of the phenomena beyond the single participant's personal experience, and it provides some explanation of the rationale for these differences. Although shadowed data need to be verified, using shadowed data provides direction for theoretical sampling, and the clues*

that it provides in tum enhances the analysis. It simply moves analysis along more quickly.

The researcher may ask the informants to consider the benefits and costs to a range of stakeholder groups. Observations of stakeholder groups are made in their natural settings for example the participants in the waiting room at CCRep, research staff at work and those attending the New Zealand Association of Clinical Research (NZACRes) conference. As each individual informant can generate many ideas, large samples are not needed to compile rich data sets (Starks et al. 2007). Many of the informants are experts in their field. Romney, Batchelder, and Wellerts (1986) find that when informants have a high level of expertise in the area of inquiry samples as small as four informants can provide data of a high confidence level. Table 4.7 presents the sampling techniques used for each stakeholder group.

TRIAL PARTICIPANTS

The current study uses purposive homogeneous sampling to identify informants for the stakeholder group of trial participants. Homogeneous sampling '*involves the selection of participants from a particular subgroup for in-depth study'* (Teddlie and Tashakkori 2009 p188). A subgroup of 24 people is randomly selected from the 250 selected for the health outcomes study to which is referred to above, for an in-depth study using four focus groups. Almost all invited trial participants agree to be part of the focus groups. Those who declined gave health-related reasons. The researcher runs four focus groups involving a total of 19 trial participants. Two family members also attended these focus groups.

The researcher also sends 100 survey forms to trial participants who are not members of focus groups. Twenty surveys are returned uncompleted due to changes in address, health or the death of the participant. Two of those who receive surveys ring and offer a telephone interview instead because health problems prevent them from completing the form. Fifteen of the addressees complete and return the survey form. Four of these informants indicate that they are both Counties Manukau community members and trial participants. Family members complete and return a further five surveys. The researcher collects further information from those who were purposively selected for other stakeholder groups but indicate they have also been participants in at least one clinical trial. The researcher collects the views of 40 trial participants.

FAMILY MEMBERS AND CARE GIVERS

Privacy considerations require that purposive snowball sampling be used to identify members of this group. In snowball sampling, existing informants - in this instance, trial participants identify family members and care givers as further study members (Teddlie and Tashakkori, 2009). Trial participants who attend the focus groups are invited to bring a family member or care giver. Two family members accept this invitation. Additional informants appear from three sources. First, five family members acting in this capacity, complete surveys sent to trial participants. Second, three members of other stakeholder groups indicate that they have also been a family member of, or a caregiver to, a trial participant. Finally, the researcher examines the written submission by a family member to the *2010 New Zealand Parliament Health Select Committee "Inquiry into improving New Zealand's environment to support innovation through clinical trials"* to identify any additional multiple stakeholder perceptions of benefits and costs. In total, the views of eleven family members and caregivers are collected.

DHB STAFF MEMBERS,

Respecting the busy workloads of hospital staff, The researcher initially uses volunteer sampling with this group. The researcher places an invitation to respond to a web-based survey on the CMDHB intranet site. As volunteer sampling can lead to bias, the researcher uses purposive confirming and disconfirming sampling (Teddlie and Tashakkori 2009) to identify individuals in a range of roles and invite them to complete the survey. As with the other stakeholder groups some staff members indicate that they fall into more than one informant category. Three of them indicate that they are also researchers and another two say that they have been participants in clinical trials. Informants in this group complete 22 on-line surveys.

RESEARCHERS

As the researcher wishes to interview research staff in the CCRep environment purposive sampling, reputational case technique is used to identify CCRep researchers. This leads to in depth interviews with two members of CCRep's research team who are suggested by the Clinical Director. Notwithstanding the potential for bias, the researcher considers this an important entrée for data collection. The researcher next seeks informants to either verify or refute patterns in the

data that have emerged in the interviews. The researcher distributes surveys through satchel inserts at the 2009 New Zealand Clinical Research Conference (as previously described, by personal invitation and by inclusion on the CMDHB intranet site). In addition, the researcher uses a convenience sample of two politicians is interviewed who have past involvement as clinical drug trial researchers. Finally, the researcher listens to verbal submissions and examines 16 written submissions to the *Health Select Committee* (2010) by researchers to identify any additional perceptions by this group. In all, informants complete 17 online surveys. When interviews, hearing submissions are summed, the number of informants for this group is 36.

THE COUNTIES MANUKAU COMMUNITY

The researcher uses purposive sampling and sends survey invitations to a range of consumer groups. For convenience, the researcher ask a captive sample of a Manukau Institute of Technology business class studying stakeholder analysis to complete the survey as representatives of the Counties Manukau Community. The researcher examines submissions from 4 individuals and 15 consumer groups to the *Health Select Committee* (2010). Members of other stakeholder groups also self-select this informant group making the total sample 42.

GOVERNMENT BODIES AND POLITICIANS,

Government bodies and politicians include central and local government politicians, elected DHB members and members of the Pharmaceutical Management Agency (PHARMAC) and the New Zealand Medicines and Medical Devices Safety Authority (Medsafe), which are both government organisations. As it is essential to gain representation from across the political spectrum and the researcher applies purposive sampling to achieve representativeness. Wherever possible the researcher approaches members of parliament across the political spectrum that lives in

the Counties Manukau District. Where this is not possible the researcher allow the political party to nominate someone to respond. PHARMAC and Medsafe are approached directly. Informants complete 10 in depth interviews and one survey, providing 11 views from across the political spectrum.

TABLE 4-7 SAMPLING TECHNIQUES USED FOR EACH STAKEHOLDER GROUP.

Stakeholder	Sampling method	Collection method	Total sample	Select	Address unknown	informants	Dual	Total
Trial participants	Probability: randomised, controlled Purposive: homogenous	Focus groups (4) Survey forms Telephone interview	250	24 10	20	19 11 2	2 6	40
Family and caregivers	Purposive: snowball	Focus Group Invite Inquiry				2 5 1	3	11
Health board staff members	Volunteer Purposive: confirming and disconfirming	Web-based survey				16	6	22
Researchers	Purposive: reputational case Purposive: confirming and disconfirming Convenience	In-depth interviews On-line surveys and Survey forms at conference (see note below) Inquiry				2 17 16	 2	37
Counties-Manukau community	Purposive: representativeness Convenience: captive sample	Survey forms Inquiry	18			16 19	7	42
Government, government bodies and politicians	Purposive: representativeness	In-depth interviews Surveys				10 1		11
Pharmaceutical industry	Purposive: reputational case Confirming or disconfirming	In-depth interviews On-line surveys and Survey forms at conference Inquiry				3 9 5		17

PHARMACEUTICAL INDUSTRY

The researcher uses two types of sampling techniques with this stakeholder group. First, the researcher uses reputational case sampling. Reputational case sampling involves selecting cases on the recommendation of a key informant. It can be difficult to contact members of the pharmaceutical industry in New Zealand because limited information is available on websites and in the phone book. The Chief Executive Officer of the Researched Medicines Industry Association (RMI, now known as Medicines New Zealand) recommended the sample for interviewing this group. Initially three in-depth interviews are conducted.

The researcher seeks additional informants to either verify or refute patterns in the data that emerge in the interviews. The researcher sends invitations to all RMI member companies to complete the on-line survey. Survey forms are included in 159 delegates' satchels at the 2009 New Zealand Clinical Research Conference held in Auckland. Conference delegates represent stakeholder groups including the pharmaceutical industry, researchers and hospital staff. Nine informants from the pharmaceutical industry complete and return surveys either on-line or by post. Finally, the researcher listens to verbal submissions and examines written submissions from five pharmaceutical companies presented to the *Health Select Committee* (2010) to identify any additional perceptions from this group. The combined total of surveys, interviews and submissions for this group is 17. I justify this relatively small sample size by the expertise of the informants. Romney et al. (1986) find that when informants have a high level of expertise in the area of inquiry samples as small as four inform ants can provide data of a high confidence level.

PROCEDURES USED

In carrying out the research design, the researcher uses several specific procedures including, focus groups, in-depth interviews, telephone interviews and surveys. These procedures are outlined next.

SEMI STRUCTURED INTERVIEWS

One of the most common forms of data collection is the interview (DiCicco-Bloom and Crabtree 2006). Interviews can take a structured, semi-structured or unstructured form (Whiting 2008). Structured interviews are most often used to collect quantitative data by asking closed questions.

Unstructured interviews are at the other end of the continuum and are similar to a guided conversation something most often used in anthropology (Whiting 2008). Semi-structured interviews use predetermined open-ended questions, with other questions emerging during the interview. Interviews are scheduled in advance at a designated time and location outside of the environment under investigation (DiCicco-Bloom, *et. al.,* 2006). Semi-structured in-depth interviews are the most widely used interviewing format for health research and take between thirty minutes to several hours to complete (Whiting 2008).

The researcher uses semi-structured-interviews to collect data from participants 'in order to find out what they do, think or feel' (Hussey and Hussey 1997 p 156). They are the preferred form of data gathering when it is important to understand the basis for the interviewee's opinions or beliefs about the matter being examined (Easterby-Smith, Thorpe and Lowe 1991). Other advantages of using this method include the opportunity to ask questions that are more complex and the opportunity to ask probing or follow-up questions to ensure understanding. However, compared to administering questionnaires an interview is time consuming and expensive, issues of participant confidentially may arise and the interviewer may have an effect on the process (Hussey and Hussey 1997). As a means of mitigating these disadvantages in this study, the researcher combines the data from interviews with data from other sources.

The researcher asks the same questions in the focus groups as she does for the interviews and surveys. Morgan (1995) suggests that individual interviews be conducted before the focus groups as a means of testing the focus group instrument, as these are cheaper and easier to schedule than focus groups. The interviews therefore are conducted at the beginning of the research. The interviews follow the same procedures as the focus groups but on a one to one basis. The interviews are recorded using a standard digital recording device.

FOCUS GROUPS

Focus groups are a method of collecting data and exploring issues. They involve interaction and discussion among participants on the issues surrounding the research problem. They are a useful means to obtain data and reach insights that would be less accessible without the interaction of the group (Webb and Kevern 2001). When participants start to act and view themselves as members of a group, their interactions change from simple everyday talk, allowing them to take on the identity of a focus group and develop a common communication ground (Hyden and

Bulow 2003). Focus groups allow participants to hear the ideas of others and use those ideas to formulate their own opinions (Krueger 1995). They capture the complexity of life's experiences and provide decision makers with valuable information (Krueger 1995).

The prepared questions provide a structure, which assist the researcher to guide the discussion, keep the conversation focused and ensure consistency between the focus groups. The questions facilitate a high depth of discussion and generate opinion as well as the exploration of related issues. When identifying costs, the researcher is interested in additional resources expended and negative outcomes resulting from clinical trials (financial and non-financial costs). Similarly, the researcher encourages the identification of benefits, which include the positive outcomes and resources leveraged over and above what would have happened if the clinical trial had not occurred (Ziller and Phibbs 203).

The researcher encourages focus group participants to discuss around the questions and provide examples from their own experiences. Group interaction tends to elicit 'mutual self-disclosure' (Morgan 1995). The researcher moves the discussion on from one topic to another as each theme is exhausted, that is nothing new is being added. Before the end of each group, the researcher summarises the main themes of the discussion for the group to confirm or correct the findings as presented.

Data derived from the focus groups is recorded on a digital recorder as a means of capturing the ideas and words used and the amount of consensus and interest that topics generate both within each focus group and across the groups (Morgan 1995). Due to the small sample size, the results may not be generalisable to the wider population (Ross, Stroud, Rose, and Jorgensen 2006). For this reason, the researcher uses other data collection methods in conjunction with the focus group method. The data is transcribed and downloaded onto NVivo 8.

SURVEYS

The researcher employs self-completion surveys as a means of data collection to supplement the data gained from interviews and focus groups. Surveys have the advantages of maintaining anonymity, being able to cover a wide geographical area in a short time and allowing informants to take more time to complete at their own convenience (Cavana, Delahaye and Sekaran 2001). Problems associated with the survey method include poor response rates leading to bias in representation, informants not understanding the questions and inability to probe for more

detailed answers (McGivern 2006). By combining, this method of data collection with other forms these disadvantages are in many respects compensated for. Surveys are posted to 100 trial participants and are inserted in the delegate satchels of those attending the 2009 New Zealand Association of Clinical Researchers conference. The survey is available on-line and the web address is printed on the survey hard copy. An invitation to complete the either the on-line survey or a paper based survey is posted on the CMDHB intranet. In addition, the researcher sends personal invitations to complete the survey to a purposively selected sample group. The electronic option for completion of the survey is used in preference to the paper based by most staff and researcher informants. The electronic survey is also more convenient for me to collate results, as data does have to be entered.

DATA ANALYSIS

The researcher begins data analysis immediately after the first interview. She continues to collect data until the analysis reaches saturation – *'the point at which no new information or themes are observed in the data'* (Guest et al. 2006, p59). She audio-records and fully transcribes the interviews and focus group discussions. She sends the transcribed data to the interviewed informant to moderate the transcript. She enters the data onto the survey web-site to give a common format for all data types collected. The researcher formats the website data and imports it onto the NVivo 8 (QSR International Pty Ltd 2007) qualitative software package. Using NVivo 8, the researcher thematically codes and analyses the data by incorporating a combination of categories derived initially from the key questions addressed in the surveys, and supplemented or refined with those that arise in the focus group discussions and interviews.

The researcher uses two methods to analyse the qualitative results. The initial analysis uses a qualitative descriptive approach. She follows this with a phenomenographical analysis. She uses a qualitative descriptive approach first to focus the attention on the informants' experiences and to allow them to report in their own words before interpretation. Phenomenographical analysis is a deep analysis, which facilitates interpretation of the meanings behind the spoken words. These processes are explained next.

The qualitative descriptive approach allows the stakeholders to express their perceptions and stories in their own words (Sandelowski 2000). Data collection is directed toward discovering the who, what, and where of experiences (Sandelowski 2000). Data collection is minimally

structured and open-ended questions, assuming that the informants' words will speak for themselves. This approach assists the current researcher to focus on the experiences of the stakeholder groups and their views on clinical trials.

The researcher next analyses the results using a phenomenographical approach. Phenomenography is a research approach used to aims to identify the qualitatively different ways in which people experience, conceptualize, perceive, and understand various kinds of phenomena (Andén, Andersson and Carl-Rudebeck 2009). Phenomenography provides a systematic way to separate and describe these differences. Marton (1986 p 31) defines phenomenography as

> *a research method adapted for mapping the qualitative different ways in which people experience, conceptualise, perceive, and understand various aspects of, and phenomena in, the world around them.*

A distinguishing feature of this approach is that the phenomenon itself is not the focus; rather the researcher focuses on how individuals perceive the phenomenon (Ireland, Tambyah, Zui Neofa and Harding 2008). The process of analysis transforms the individual perceptions to conceptions, which apply to a larger group. The outcomes of phenomenographic research are different content-related categories, which describe the differences in perceptions of the phenomena under study. Ireland et al. (2008 p12) outline the process of phenomenographic data analysis, which they suggest (p12)

> *can deliver an outcome space to a research project, which is a window to the subjects' experience of the phenomenon that is faithful to their experience as well as being rigorous in its research approach.*

Their process involves (1) familiarisation with the text to identify emerging concepts which they call "utterances", (2) Reviewing and grouping utterances into "pools of meaning", (3) assigning descriptive labels to each pool of meaning to establish "concepts" or ways in which informants experience the phenomena under study and (4) sorting and grouping together concepts into "description categories" which together form the "outcome space". This outcome space becomes a picture of the phenomenon under investigation.

The researcher uses NVivo 8 to assist this process. The researcher codes each source document (individual informant) as a case with an independent case number. The researcher codes cases according to survey questions to allow comparison of informant answers to individual questions. The researcher codes costs and benefits for each stakeholder group separately and then cross-

references them to identify items that are a cost to some informants and a benefit to others. The researcher uses this process to compare both the responses from members of the same stakeholder group and those across stakeholder groups. Initial familiarisation of each case includes reading, reflecting and coding onto free nodes. The researcher establishes pools of meaning by annotating, memoing, and discussing. The researcher develops concepts by linking, visualising and recoding onto tree nodes. Further examination of the tree nodes result in the finalisation of the descriptive categories.

An example of this process is seen in the exploration of the impact 'Adverse Events' First the researcher downloads the individual informant source onto NVIVO and codes them onto nodes (1) according to the question answers and (2) by whether adverse reactions are identified. This provides information on whether the informant perceives the adverse reaction as a cost or benefit and to whom that cost or benefit applies. Next, the researcher expands the benefit and cost nodes further by adding tree nodes. The cost node expands into nodes describing the nature of the cost for example (1) participant health, (2) treatment cost, (3) lost reputation and (4) effect on future research. The researcher further codes these categories along the tree nodes for example, participant health is coded as having impacts that are further coded as being either (1) long-term or (2) short-term. She creates a shorter tree for benefits of adverse events, which relate to individual stories. The researcher further links these stories to a tree that identifies case examples of adverse events. Case examples are divided into those the informant experiences directly and those that the informants has read or heard about.

Mapping the above information identifies a number of insights. Of all the stakeholder groups participants are the least worried about adverse events and some participants even view adverse events as a benefit. Family members are concerned about adverse events and in many instances; they base their concerns on adverse reactions they read in the media. That research staff are more conscious of the possible hidden long term adverse events that may occur (eg adverse events that may present long after the trial is finished). Adverse events are seen as a cost to the participant, family and care giver, researcher, health board, pharmaceutical company and to society as a whole.

ETHICAL ISSUES

This study has ethics approval from (1) the Tasmania Social Sciences Human Research Ethics Committee (Ethics Ref No: H10522) (2) the Counties Manukau District Health Board Maori Research Review Committee (3) the Northern Regional Health Ethics Committee (nty/09/04/037) and (4) The Manukau Institute of Technology ethics committee REF: E09/EXP/19 (see appendix 1). In addition, because this research involves highly commercially sensitive information the researcher negotiates a detailed data transfer agreement.

SUMMARY AND CONCLUSION

This chapter explains the methods used in a simultaneous parallel multi-strand mixed methods designed study to analyse the benefits and costs of conducting sponsored clinical trials in a publicly funded New Zealand hospital. It involves three strands: (1) a health outcomes strand involving a retrospective cohort study of participants in sponsored clinical trials, (conducted by staff at CCRep and reported separately) (2) a multiple stakeholder perceptions outcomes strand assessing stakeholder multiple stakeholder perceptions of clinical trials being performed at CMDHB and (3) an economic outcomes strand evaluating the benefits costs of clinical trials. The researcher utilises both qualitative and quantitative methods to bring breadth and depth to the research.

A blend of methods provides a rich and powerful means of evaluating the benefits and costs of clinical trials. In the multiple stakeholder perceptions strand, the researcher conducts focus groups, interviews and semi-structured surveys to explore the perceptions of a variety of stakeholders. The economic outcomes strand draws on the health outcomes strand and from other sources to estimate the benefits and costs of clinical trials. The researcher collects both quantitative and qualitative data in the interests of robust research findings. While the data do not support triangulation between the qualitative and quantitative methods, the qualitative data analysis complements the quantitative data analysis. Collectively, the results provide complementary evidence and contribute to a comprehensive understanding of the outcomes of clinical trials in New Zealand.

The thesis continues as follows. The next chapter, chapter 5 reports the quantitative results from the economic outcomes strand of the current study. Chapter 6 reports the qualitative results from

the studies multiple stakeholder perceptions strand. Chapter 7, the final chapter, presents the studies summary and conclusions.

5. RESULTS FROM THE ECONOMIC OUTCOMES STRAND

As stated in chapter 1, the objective of the current study is to answer the question: 'What is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?' Chapter 1 introduces the reader to the key characteristics of the current study. Chapters 2 and 3 review the theoretical and empirical literature that provides the foundation of the current study. Chapter 4 explains the methodology and methods used in the analysis. This chapter, chapter 5 reports on the results of the economic outcomes strand of the mixed methods study. Chapter 6 reports on the results of the multiple stakeholder perceptions strand. Chapter 7 concludes the thesis with a review of its principal findings and associated conclusions, an overview of its contributions, and e recommendations for future research.

The empirical study outlined in the chapter 4 applies a BCA to analyse the value of conducting clinical trials in a publicly funded New Zealand hospital. The economic outcomes strand of the current study determines the size and distribution of the benefits and costs of the two Phase III clinical trials from three points of view (1) CCRep, (2) CMDHB, and (3) New Zealand society. Participants for the two trials were recruited between 2001 and 2003 and the clinical trials were completed in 2007, although participants continued to attend follow-up appointments until June 2009.

MICRO-LEVEL: BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF CCREP

As described in chapter 4, the researcher first considers the costs, revenue and surplus for clinical trial 1 (Table 5.1) and clinical trial 2 (Table 5.2) using the perspective of CCRep.

TABLE 5-1 ANALYSIS OF CLINICAL TRIAL 1.

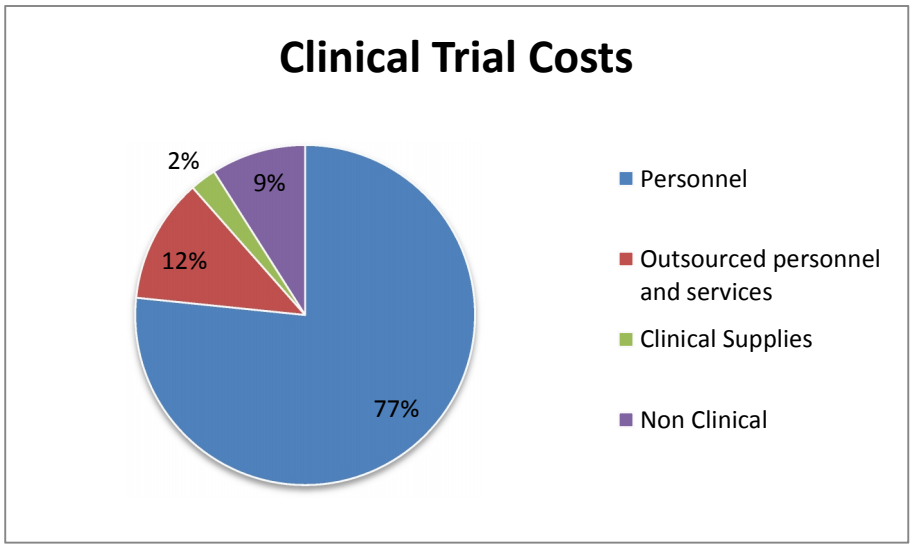
	Recruitment		**Study Period**				**Follow-up**	
Year	1	2	3	4	5	6	7	8
TOTAL REVENUE	40,306	204,649	129,547	69,689	92,058	191,962	74,646	9,245
Personnel	28,122	103,197	85,059	57,730	59,352	78,258	84,639	1,909
Outsourced Services	(8,684)	23,974	47,063	5,997	1,627	4,974	1,797	947
Clinical Supplies	1,265	67	1,062	5,627	4,583	3,546	3,067	-
Non Clinical	1,232	11,833	7,172	3,348	7,170	11,900	19,273	2,059
NET SURPLUS	18,371	65,578	(10,809)	(6,938)	19,325	93,284	(34,129)	4,331
Surplus per person /136	**135**	**482**	**(79)**	**(51)**	**142**	**686**	**(251)**	32
NPV @ 0%	**$1,102**							
NPV @ 3.5%	**$974**							
NPV @ 5%	**$926**							
NPV @ 10%	**$791**							

TABLE 5-2 ANALYSIS OF CLINICAL TRIAL 2.

	Recruitment		Study Period				Follow-up	
Year	1	2	3	4	5	6	7	8
REVENUE	-	124,331	41,267	42,030	30,486	28,216	15,912	10,956
Personnel	14,379	34,810	29,532	24,836	25,350	28,909	19,212	396
Outsourced	-	3,763	4,082	1,685	732	255	3,230	10,144
Clinical Supplies	229	7,450	(8,229)	1,469	670	965	298	-
Non Clinical	513	5,543	1,214	1,624	1,476	2,118	1,369	761
NET SURPLUS	(15,121)	72,765	14,667	12,416	2,257	(4,031)	(8,196)	345
Per person surplus/116	(130)	627	126	107	19	(35)	(71)	192
NPV@0%	$836							
NPV @ 3.5%	$745							
NPV @ 5%	$711							
NPV @ 10%	$613							

COSTS

FIGURE 5-1PERCENTAGE CLINICAL TRIAL COSTS FOR THE TWO STUDY TRIALS.



The two trials show similar distributions of costs (see figure 5.1). The costs of personnel make up the largest proportion of costs at 77 percent, outsourced personnel and services represent 12 percent, non-clinical items 9 percent and the final 2 percent clinical supplies. Table 5.3 lists the items included in each cost categories.

FIGURE 5-2 AVERAGE COST PER PARTICIPANT FOR THE TWO CLINICAL TRIALS.

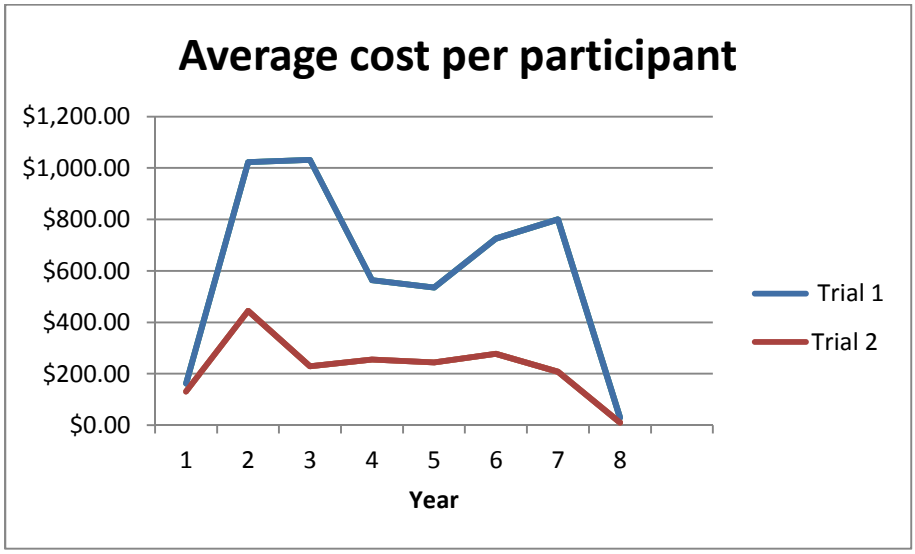


TABLE 5-3 COST CATEGORIES USED IN THE MICRO-LEVEL ANALYSIS

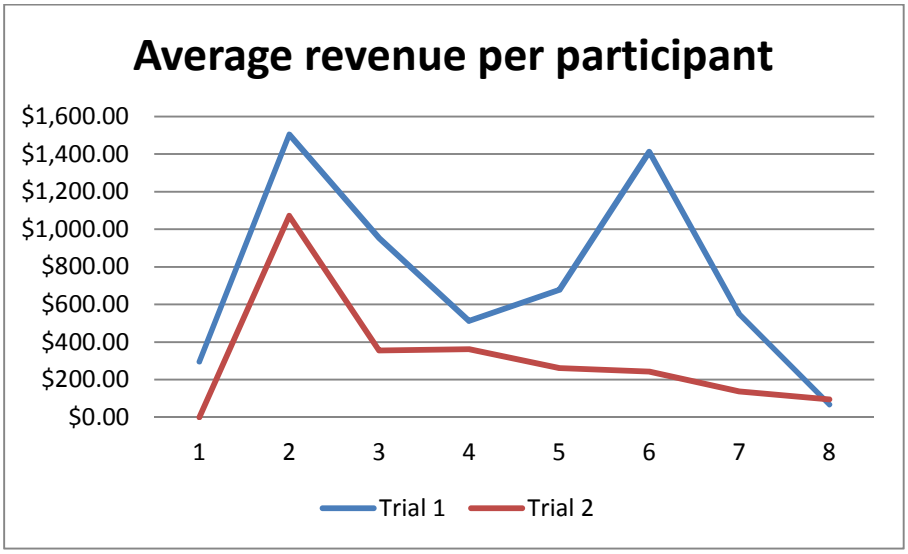
Cost category	Details
Personnel	Salaries for senior medical officers, registrars, nurses, managers, administration, clerical and secretarial staff
	Accident Compensation Commission (ACC) Levies
	study fees, courses and conferences
Outsourced personnel and services	'fee for service' medical officers
	laboratory services and send-away test
	radiology services
	provider auditing and monitoring
Non-clinical items	rents
	external storage services
	fuel
	taxis
	staff travel, accommodation and meals
	information technology depreciation
	hardware purchases less than $500
	telecommunications
	insurance
	printing and forms
	Stationery, supplies and other office expenses
	postage courier and freight
	books, periodicals and journals
	advertising
	staff relations and support
	sundry
clinical supplies	containers and bags
	continence and hygiene supplies
	dressings
	protective clothing
	patient consumables
	electrodes
	recording paper, tapes and disks
	monitoring equipment and other diagnostic supplies
	batteries,
	clinical equipment
	minor purchases
	patient welfare, incentives, lodgings and transport

Figure 5.2 presents the average cost per participant for the two clinical trials. The average cost per participant (ACP) is higher for trial 1 than for trial 2 and the ACP per year is highest for both trials during the recruitment period. The ACP per year decreases during the trial period though the ACP per year shows a second peak at the end of the trial, leading into the follow-up period. This second peak is more pronounced in trial 1.

REVENUE

Revenue for the two trials is received from the sponsors. It generally follows the pattern of costs (see figure 5.3). Trial 2 costs were incurred in 2001, although revenue was received only in 2002, which resulted in a loss in the 2001 period. The sponsor makes larger payments at the start of the trial when costs are highest. Trial 1 also has a larger payment in 2006, which compensated the extra costs experienced at the end of the trial period.

FIGURE 5-3 AVERAGE REVENUE PER PARTICIPANT FOR EACH YEAR OF CLINICAL TRIAL.

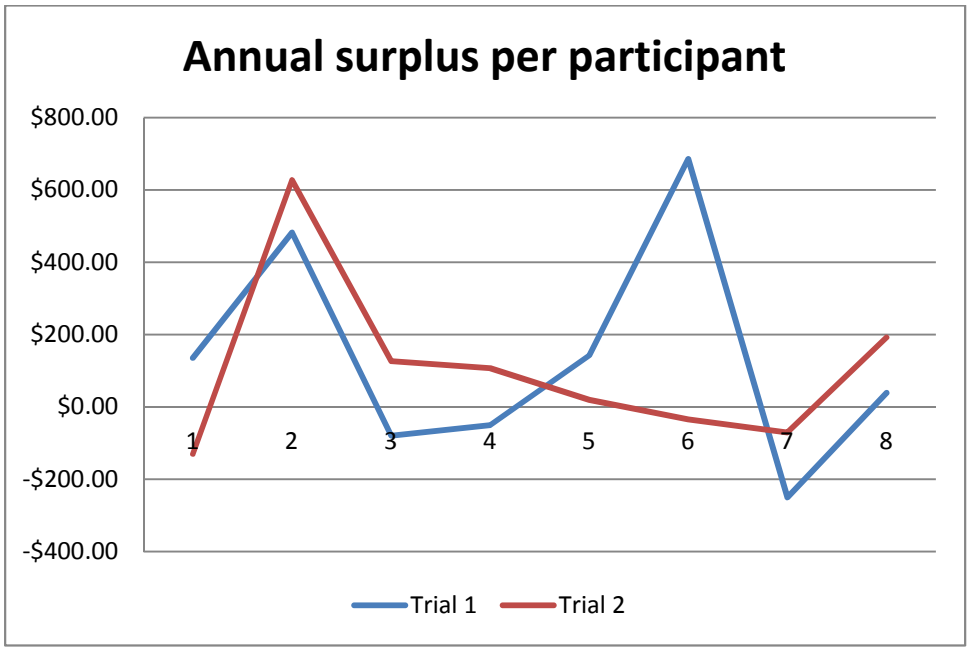


COST AND REVENUE STREAMS

Figure 5.4 shows the average annual cost and revenue streams resulting in a surplus for the period of the trials. In addition to considering average annual surplus, the researcher separates the data into three periods: (1) recruitment, years 1 and 2, (2) trial, years 3, 4, 5 and 6 and (3) follow-up, years 7 and 8. This allows the identification of any difference in cost and revenue streams between periods. The initial recruitment begins in June 2001 and the follow-up period

ends in July 2009. The average surplus per trial participant after considering costs and revenue is highest in 2002 after recruitment has begun. This is consistent across both trials. In trial 1, a second peak occurs at the end of the trial and prior to the follow-up period. The trial period produces the lowest surplus for both trials under investigation. The cost revenue stream for trial 1 dips below zero during the trial period in year 3. It again dips below zero for both trials at the start of the follow-up period in year 7. These peaks and troughs indicate that careful management is critical to ensure cash is available as needed.

FIGURE 5-4 THE AVERAGE ANNUAL COST AND REVENUE STREAMS PER PARTICIPANT FOR CLINICAL TRIALS 1 AND 2.



The next task is to discount the benefits and costs to obtain net present values. If the NPV is greater than zero at the applicable discount rate, the activity is worth undertaking and *ceteris paribus*, a program with a higher NPV is better than a program with a lower NPV (Heald, 2002). The surplus for each year of the trials, discounted back to 2001 using the discount rate of 3.5 percent is $974.37 per trial participant for trial 1. The researcher also conducts a sensitivity analysis using discount rates of 0 percent, 5 percent and 10 percent (as discussed in chapter 4). The NPV per person for trial 1 ranges from $1,102.66 at 0% to $791.49 at 10% (see Table 5.1). Trial 2 produces a slightly smaller positive return of $745.24 per participant (NPV at 3.5 percent) and ranges from $836.34 at 0% to $613.74 at 10% (see Table 5.2). This makes both trials

worthwhile from the perspective of CCRep particularly when the rate per person is multiplied by the number of participants in the trials and by the number of trials being conducted by CCRep. Clinical trial 1 has 136 participants and trial 2 has 116 participants. These trials were two of the six trials in CCRep conducted in 2001 (rising to 70 trials by 2008).

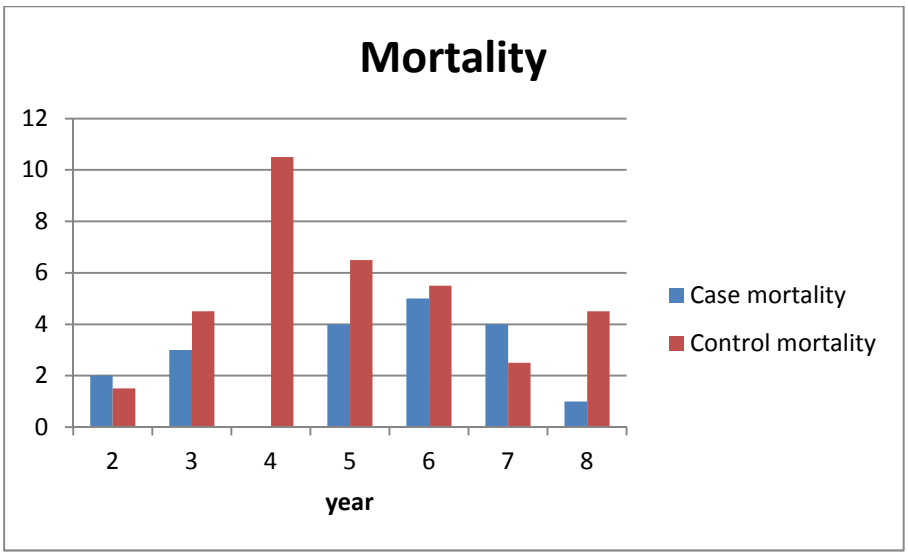
It is difficult to compare the results of the micro-level analysis with those of other published studies, as there is no uniform format for collecting cost data. For example, Evans, Dahrouge et al. (2000) find data management costs contribute to twenty-one percent of total costs but the difference between data management costs and personnel costs is unclear.

MESO-LEVEL: BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF CMDHB

There are three key differences between the meso-level analysis and the micro-level analysis from the perspective of CMDHB. First, the researcher merges the participants from two separate trials in the micro-level study into one group, the case group (see figure 5.3). Second, the researcher compares the case group with a matched-control group who receive standardised care. Third, the researcher adds into the analysis the CMDHB budget impacts, which result from clinical trial activities. In particular, the researcher considers the costs and savings from pharmaceutical and laboratory subsidies, patient treatment programmes, capital costs, and indirect costs funded by CMDHB.

Finally, the researcher adjusts the analysis to take into account the differing mortality levels between case and control groups using data from the health benefits study. Fireman et al. (2002) find that when comparing case and control group costs in the post one-year period, cost differentials between them are influenced by recurrence (when a condition reappears after a period of time during which it could not be detected) and mortality. Figure 5.5 shows that the different rates of mortality for the case and control groups. The researcher determines the actual number of life years saved per year for the case and control groups from the mortality rates and halves this number in the control to recognise the difference between the size of the case group (n=252) and the control group (n= 504). The researcher accounts for differences in mortality rates by subtracting the annual mortalities for the case group from those of the control group in each year of study.

FIGURE 5-5 MORTALITY RATES FOR CASE AND CONTROL GROUPS*.



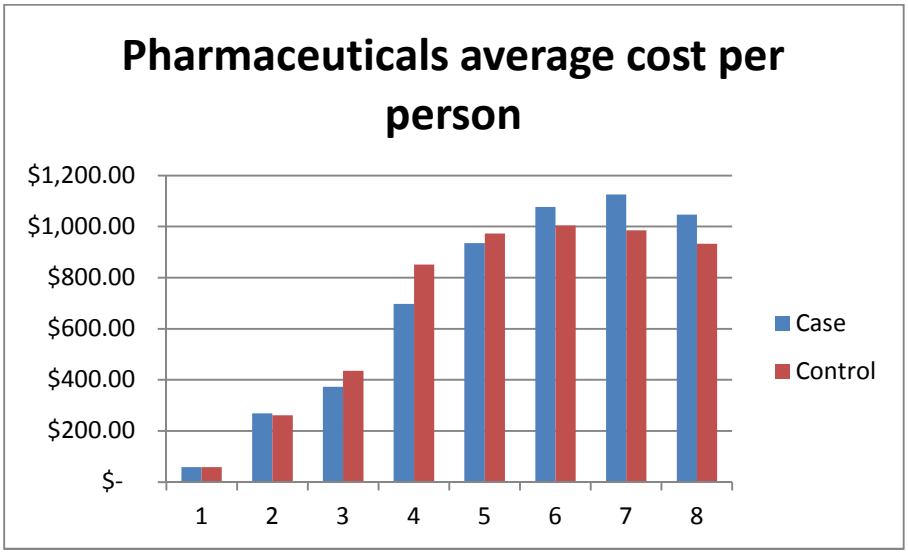
*. Control group mortality has been adjusted for different sample sizes (sample size for case = 252, sample size control = 504. In year 4 case group mortality = 0)

PHARMACEUTICALS

The trial sponsor provides the pharmaceuticals used in the trial free of charge. CMDHB continues to pay for pharmaceuticals that are not essential for the trial. The researcher uses the pharmaceutical 'cost ex supplier' data from the Ministry of Health (MOH) Pharmaceutical Claims Data Mart for both case and control groups. These data provide the total cost of medications issued minus goods and services tax (GST) for the case and control groups for each of the study years. In comparing the cost of pharmaceuticals for the case group with that of the control group, differences in mortality rates are accounted for by subtracting the annual mortalities for the case group from the control group for each year of study. The researcher then calculates an average pharmaceutical cost per person per year (see figure 5.6). The researcher subtracts the average pharmaceutical cost per person per year for the case group from the control group to find the average per person per year cost difference. The results show the savings per person from pharmaceutical cost avoidance is achieved in only three years (2003, 2004 and 2005) over the study period. The rest of the time the average per person costs for the case group are higher than for those of the control group, which represents cost increases for CMDHB. Using a NPV at 3.5 percent to discount back to the base year of 2001. The researcher finds the

average per person annual pharmaceutical costs are $39.69 for the case group over the control group this equates to an overall $3,680.84 higher cost for the case group over the control group.

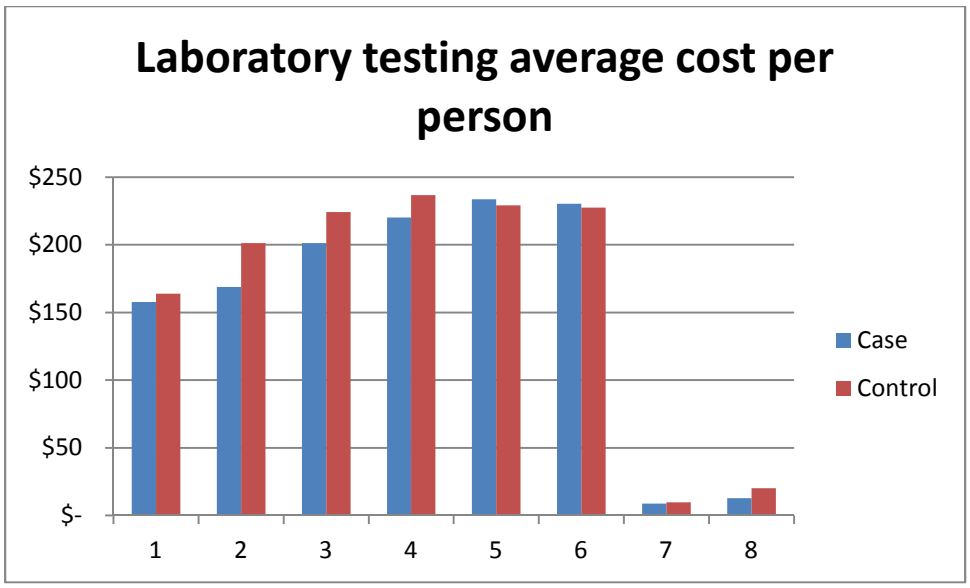
FIGURE 5-6 AVERAGE PHARMACEUTICALS COST PER PERSON FOR CASE AND CONTROL GROUPS.



LABORATORY TESTS

The sponsor pays for all laboratory tests required for the trial. Laboratory tests other than those required as part of the trial protocol remain the responsibility of CMDHB. The researcher uses the MOH 'Laboratory Claims Data Warehouse' (Labs) to access laboratory costs charged to CMDHB for the case and control groups. This source provides claim and payment information for laboratory tests that have been processed by the MOH General Transaction Processing System (GTPS). The researcher uses the Labs 'Amount paid EXCL' data. This data element provides the amount paid to the laboratory by Ministry of Health for performing laboratory tests, exclusive of GST. The researcher uses the same method for analysing laboratory costs and savings as outlined above for the analysis of pharmaceutical costs and savings.

FIGURE 5-7 LABORATORY TESTING AVERAGE COSTS PER PERSON FOR CASE AND CONTROL GROUPS.*.



*A new laboratory-testing contract came into operation in 2007 resulting in pricing changes[1]

The researcher accounts for differences in mortality rates by subtracting the annual mortality numbers for the case group from the control group for each year of the study. The researcher then calculates the average per person annual laboratory test cost (figure 5.7). The researcher subtracts the average per person annual case laboratory tests cost from the average per person annual control cost to find the average per person annual cost difference for each of the trial years. The researcher finds a drop in the average per person annual laboratory testing costs in 2007, which the researcher attributes to a change in contractor for laboratory testing within the Auckland region[3]. In the recruitment period and the trial period until 2005, the researcher finds that the average per person annual laboratory test costs is higher for the control group than the case group. In the later stages of the trial, this trend is reversed with the average per person annual laboratory test cost for the case group exceeding that of the control group. Overall when discounted back to 2001 the researcher finds that CMDHB has a net gain from avoiding

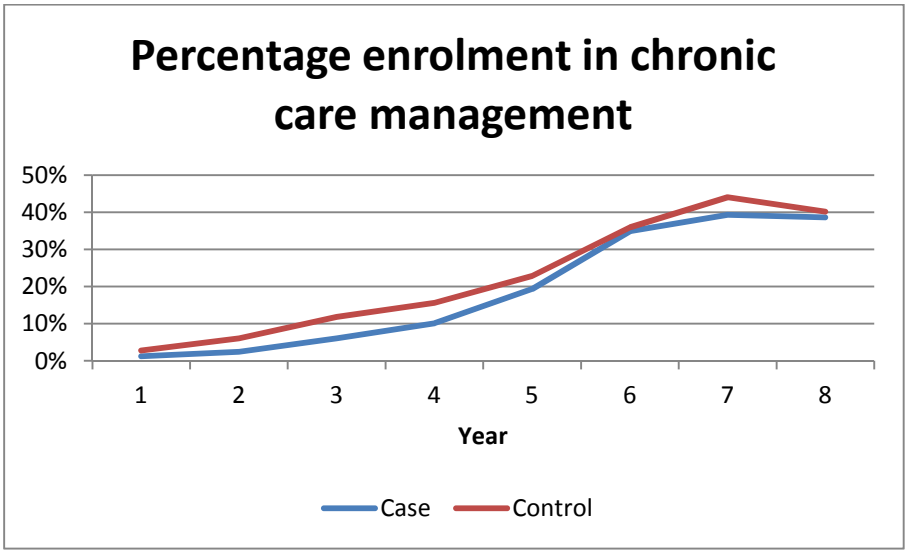
[3] In 2007 the three regional DHBs in Auckland entered into a new contract with Labtests Auckland Ltd to provide community laboratory services in the region. The total savings for the Auckland region following the new contract was estimated at $15million each year (Auckland District Health Board, 2006)

laboratory costs for those participating in the clinical trials. The NPV for the average per person laboratory cost avoidances using a discount rate of 3.5 percent is $71.54 this equates to an overall total cost avoidance of $17,740 for the two trials.

CHRONIC CARE MANAGEMENT COSTS (CCM)

As noted earlier, there is no central database that provides information on the cost of outpatient care for members of this study and control groups. CMDHB does however have a Chronic Care Management (CCM) program for high need chronic care patients within CMDHB. As these are the only data available on the cost of outpatient care for patients with similar conditions to the case group and as some of the case and control group are enrolled in this program the researcher relies on CCM to measure outpatient cost avoidance. The researcher finds that the number of enrolments from the control group exceeds that of the case group throughout the study period (see figure 5.8).

FIGURE 5-8 PERCENTAGE OF CASE AND CONTROL GROUP ENROLMENTS IN CHRONIC CARE MANAGEMENT



.

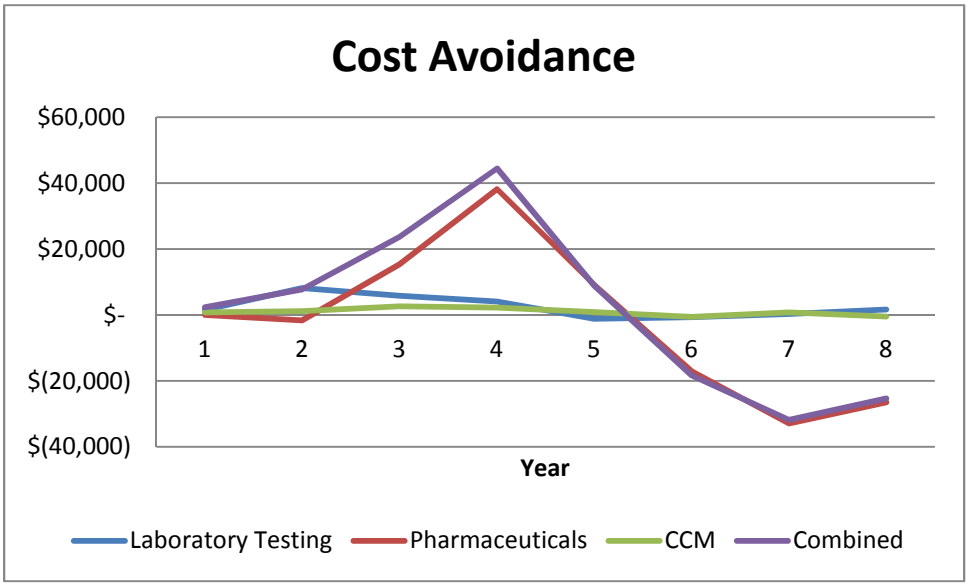
In 2009 the percentage enrolments for the control group is about 44 percent and that for the case group is about 41 percent. Watson (2006) asserts that clinical trial participants are effectively removed from the public health system for the duration of the trial. The results of the current study suggest this assertion is incorrect and that participants of clinical trials attend outpatient appointments within the public health system. When the researcher discounts the results back to

the base year of 2001 at a discount rate of 3.5 percent the savings attributable to the cost avoidance from CCM is $6,606.

COMBINED SAVINGS FROM COST AVOIDANCE

Figure 5.9 show that a comparison of the cost avoidance for pharmaceuticals, laboratory testing and CCM as well as the total savings from cost avoidance. CMDHB benefits from cost avoidance until the end of the trial period in 2006. CMDHB incurs additional costs for the case group when compared to the control in 2006 and this loss continues through the follow-up period. Overall, there are benefits for CMDHB from cost avoidance. Savings discounted to 2001 at a discount rate of 3.5 percent and indicates a net benefit for CMDHB from cost avoidance of $17,675.

FIGURE 5-9 COMPARISON OF SAVINGS DUE TO COST AVOIDANCE FOR CMDHB.



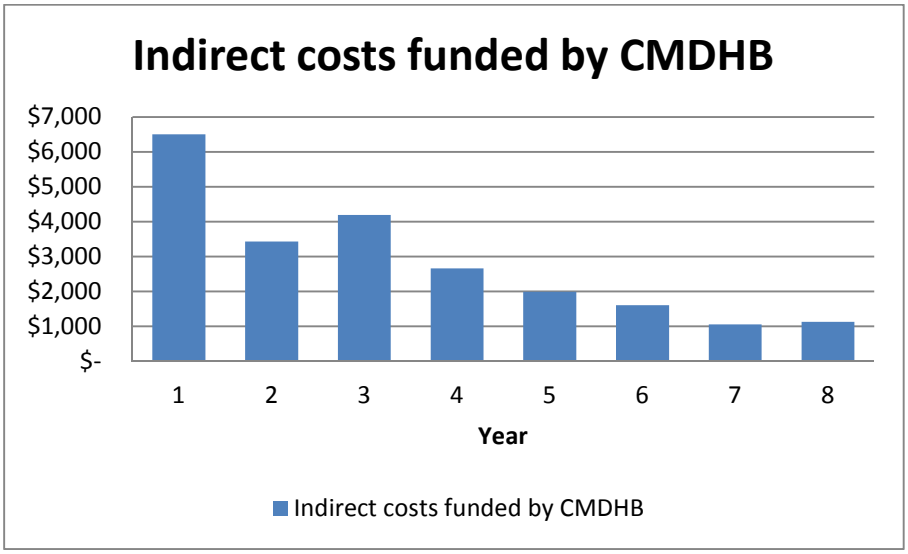
INDIRECT COSTS FUNDED BY CMDHB

The researcher draws from financial records supplied by CMDHB to establish indirect costs funded by CMDHB. The CMDHB cost allocation policy defines direct costs as *those costs directly attributable to an output class and indirect costs as those costs that cannot be identified in an economically feasible manner with a specific output class* (Counties Manukau District Health Board, 2009b p28). The CMDHB traces direct costs to output classes and allocates indirect costs to output classes based on cost drivers and related activity and usage information. Using data from financial records supplied by CMDHB the study allocates indirect costs funded

by CMDHB according to the number of trials conducted at CCRep for each year of the trial period.

Trials 1 and 2, the focus of this study, were two of the first trials conducted at CCRep following its formation in 2001. CCrep conducted only six trials in 2001. Over the period, 2001 – 2009 CCRep steadily increased the number of trials it conducted. By 2008, CCRep was running 70 trials. Economies of scale results in the lowering of the indirect costs funded by CMDHB and allocated to trials 1 and 2 over the trial period (see Figure 5.10).

FIGURE 5-10 INDIRECT COSTS FUNDED BY CMDHB AND PROPORTIONED TO TRIALS 1 AND 2.



RESULTS OF BENEFIT COST ANALYSIS CMDHB

The researcher combines the data from the CCRep benefit cost analysis with the savings from pharmaceuticals, laboratory testing and chronic care management cost avoidance. The researcher then subtracts the indirect costs funded by CMDHB to analyse the benefits and costs from the perspective of CMDHB (Table 5.4).

The researcher discounts to the base year of 2001 at a discount rate of 3.5 percent to obtain a benefit for CMDHB of $219,520 over the two trials or $871.11 per participant. To account for the uncertainties within this study a one-way sensitivity analysis is conducted. The researcher initially varies the value for cost avoidances by plus or minus 5 percent and find this alters the NPV of the BCA from the perspective of CMDHB by plus or minus $1514 or 0.69% (Table 5.4). The researcher further increases the value of cost avoidance to plus or minus 15 percent and find

TABLE 5-4 BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF CMDHB.

	Trial Recruitment		Trial				Follow-up	
Year	1	2	3	4	5	6	7	8
Net Surplus from CCRep	3,250	138,344	3,858	5,478	21,583	89,253	(42,325)	15,076
Cost avoidance	2,317	7,687	23,839	44,412	8,988	(18,749)	(15,661)	(25,476)
Total Benefits	5,567	146,030	27,697	49,890	30,570	70,504	(57,986)	(10,400)
Indirect costs funded by CMDHB	6,502	3,434	4,192	2,665	1,989	1,604	1,059	1,126
Total Costs	6,502	3,434	4,192	2,665	1,989	1,604	1,059	1,126
Total Benefit Minus Total Costs	**(935)**	**142,596**	**23,506**	**47,225**	**28,582**	**68,901**	**(59,045)**	(11,526)
NPV at 0%	$239,304							
NPV at 3.5%	$219,520							
NPV at 5%	$211,652							
NPV at 10%	$187,877							

One way sensitivity analysis varying cost avoidances by	-15%	-5%	0	+5%	+15%
Change to CMDHB CBA NPV at 3.5%	$214,979	$218,006	$219,520	$221,034	$224,062

this alters NPV by plus or minus $4,541 or 2.07%. The researcher next performs a sensitivity analysis on the discount rate by varying it to include 0 percent, 5 percent and 10 percent, which creates a range of net benefits between $239,304, and $187,877 ($745 to $949 per participant). Although these figures are much smaller than the researcher anticipated, they do suggest that the clinical trials under investigation provide a cost effective treatment option from the perspective of CMDHB.

MACRO-LEVEL: BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF NEW ZEALAND SOCIETY

Table 5.5 displays the BCA from the perspective of New Zealand society. The researcher uses QALY as a measurement of the societal benefits from clinical trials. PHARMAC (2005 p 37) recommends '*Health-related quality of life (HR-QOL) should be measured using Quality-Adjusted Life Years (QALY) as they are simple to calculate, universally used, and have face validity*'. Quality of life (QOL) can be measured on a utility scale incorporating tariff values where full health has a score of 1.0 and being dead has a score of 0. Negative scores are used to indicate health states considered worse than death (Gold, Patrick, Torrance, Fryback, Hadorn, Kamlet, Daniels and Weinstein 1996). PHARMAC (2005) recommends the New Zealand EQ-5D Tariff 2 scores when assessing QOL in New Zealand studies. The EQ-5D is a standardised instrument for use as a measure of health outcome. The EQ-5D instrument consists of two parts: five questions relating to distinct dimensions of a patient's functional capacity (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) on each of which three responses are possible, and a visual analogue scale (VAS) on which patients self-rate their current health state. The researcher combines the functional capacity score with weightings derived from a sample of the general population to provide a time-trade-off (TTO) utility score (Dolan, 2000; Dolan, Gudex, Kind and Williams 1995). The researcher uses the TTO to assess how long a period in a state of perfect health is equivalent to the given period of ill health of the trial participants. The value of utility is assessed by converting a year in a given health status to its equivalent in a state of perfect health (Morimoto and Fukui, 2002).

The researcher seeks QOL studies that match this study group of men and women aged under fifty-five years of age, at high risk of cardiovascular events whose condition is managed by medication. Although the researcher cannot find tariff rates that match the requirements

precisely, the researcher seeks tariffs relating to type II diabetes because a high percentage of the participants have type II diabetes. In one study, Clarke, Gray and Holman (2002) administer the EuroQol EQ-5D instrument to 3667 patients with type II diabetes and then estimate the impact of major complications on (1) the visual analog scale (VAS) and (2) the EQ-5D utilities derived from population-based TTO values. They establish tariff values for myocardial infarction as 0.94 and ischemic heart disease as 0.91. Bagust and Beale (2005) observe an illness controlled by taking medication is unlikely to be strongly associated with the EQ-5D dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety / depression). Some authors have suggested alternative systems for identifying tariff utility scores. For example, Huang, Brown, Ewigman, Foley and Meltzer (2007) use questionnaires to quantify 701 adult patients' tariff utilities for diabetes related complications and treatments. They find that the majority of patients rate life with treatments as close to perfect health, which they suggest indicates that patients do not regard treatments as burdensome. However, they also find that a small group of patients (10 – 18 percent) who perceive that life with treatments is a significant burden on their quality of life. They find median tariff values for conventional blood pressure control (one or two treatment agents) at 0.95 and intensive blood pressure control (three to four blood pressure agents) at 0.90. The researcher sets the tariff utility rating at 0.92, that is, the average of the above studies.

. The value of a statistical life (VSL) is an estimate of the monetary value society places on reducing by one the average number of deaths (Australian Government 2008). Access Economics (2008b pg. 16) explain the origin of VSL.

> *The terminology 'statistical' life evolved in an attempt to distinguish the value of the life of an anonymous or unknown individual from the life of a known or particular person, since identified lives are sometimes perceived to be of more value than unidentified ones.*

Debates concerning the relationship between age and VSL are common in economic literature (see for example Viscusi and Aldy 2003, Jenkins, Owens and Wiggins 2001). Although Rosen (1988) finds a relationship between age and VSL scores Viscusi and Aldy (2003 p67) identify some ambiguities in these connections

> *Based on Rosen's life cycle model, one would expect that the marginal value of another year is greater for an elderly person than for a middle-aged person but that the value of all future years declines with age for a given individual. Accounting for health status may*

> *counter the effect of increasing marginal values for a one-year life extension for an elderly person. If health status is decreasing in age, then it may be ambiguous whether the marginal value of another year increases with age.*

The effect of the age of the trial participants (participants are aged under 55 years old) and the small addition to life expectancy considered in this study may not have a major influence on the value of SLY. As the study uses QALY to account for changes in health status the researcher does not make further adjustment for age.

The researcher follows PHARMAC's (2005) advice and does not include indirect costs to patients (such as those costs relating to lost productivity of a patient due to treatment, illness or death, or that of family members if they attend to patients) in the BCA from the perspective of New Zealand society. As PHARMAC (2005 p 49) explains the loss to society from lost productivity may be negligible.

> *The actual production loss for society from sickness is likely to be much smaller than the estimated value of potential production lost. For short-term absences, a person's work may be covered by others or made up by the sick person on his/her return to work. For long-term absences, an individual's work can be covered by someone drawn from the unemployed. Therefore, while absence from work may cost the individual or employer, it may not cost society very much.*

To calculate benefits and costs of clinical trials from a societal perspective the researcher first determines the actual number of life years saved per year for the case and control groups from the health benefits study. The researcher then halves the actual life years saved, in the control group, to take into account the difference between the case group (n=252) and the control group (n= 504). The researcher subtracts the life years saved in the case group from the control group to obtain the statistical life years (SLY) saved for each year of the trial. The researcher calculates a cumulative total of SLYs saved over the time of the trial.

The researcher conducts an extreme scenario sensitivity analysis that produces two results showing possible high and low values for QALY (Briggs and Gray, 1999). The first analysis uses the QALY estimate from an Access Economics study (Access Economics, 2008b) to produce a plausible but high value for QALY. The second analysis identifies the average value of investment per QALY made by PHARMAC to produce a plausible lower range value for QALY. These methods are explained in detail next.

Access Economics estimate the VSL for New Zealand in 2008 at NZ$7,998,102. As the health outcomes strand of the clinical trials study produces data on the years of life saved rather than whole lives it is necessary to calculate the Value of a 'Statistical' Life Year (VSLY) based on the VSL. The researcher calculates the value of a statistical life year (VSLY) as a constant annual amount of the discounted value of VSL. Access Economics (2008b) estimate the VSLY for New Zealand as $335,939. The researcher follows the methodology used by Access Economics (2008b) and discount the VSLY by 3 percent to identify the VSLY for each year of the study. Finally, the researcher values health gains by multiplying the total number of QALY averted in each year by VSLY.

Value of health gains = VSLY x SLY saved x QOL Tariff. Figure 5.11 shows that the value of the QALY savings over the period of the trial. The researcher finds that QALY savings over the period of the trial produces a NPV at a discount rate of 3.5 percent of $17,384,641. The researcher performs a second sensitivity analysis using a discount rate of 0 percent, 5 percent and 10 percent, which creates a range of net benefits between $12,812,638 and $20,723,498. This method of calculating the value of QALY produces "exceptional returns" (Access Economics 2008a) for society investment in clinical trials. It may not however reflect societies' ability or willingness-to-pay for QALY gains. The researcher therefore recalculates the value of QALY gains using the payments per QALY made by PHARMAC for new investments in health technology.

FIGURE 5-11 THE VALUE OF THE QALY SAVINGS OVER THE PERIOD OF THE TRIAL

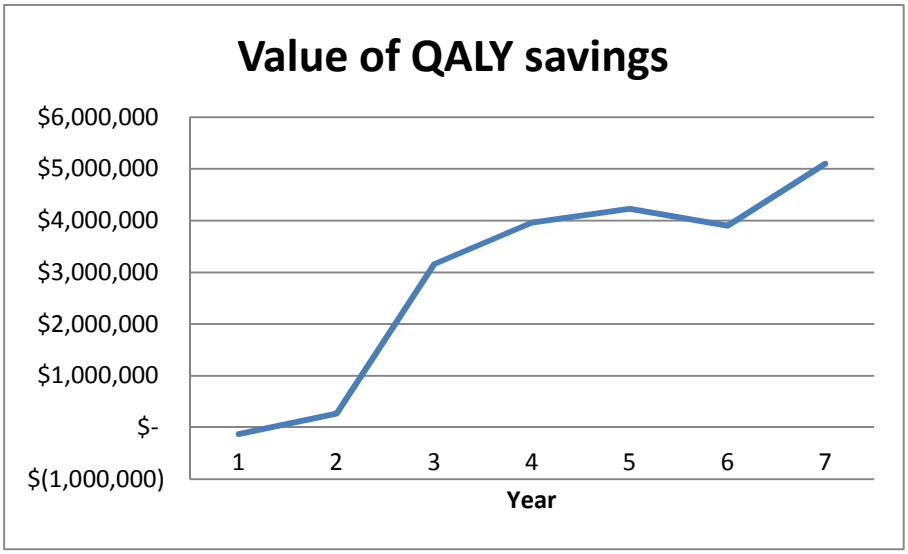


TABLE 5-5 BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF NEW ZEALAND SOCIETY.

	Recruitment		Trial				Follow-up	
Year	1	2	3	4	5	6	7	8
Cash Flow (CMDHB perspective)	(935)	142,596	23,506	47,225	28,582	68,901	(59,045)	(11,526)
Control mortality	3	9	21	13	11	5	9	
Control mortality/2	1.5	4.5	10.5	6.5	5.5	2.5	4.5	
Case mortality	2	3	0	4	5	4	1	
Statistical life years (SLY) saved	(0.5)	1.5	10.5	2.5	0.5	(1.5)	3.5	
Cumulative total SLY saved	(0.5)	1	11.5	14	14.5	13	16.5	
SLY saved x Tariff 0.92	(0.46)	0.92	10.58	12.88	13.34	11.96	15.18	
Discounted VSLY (Using base year 2008 and average 3% inflation)	281,563	289,972	298,633	307,552	316,737	326,197	335,939	
Analysis 1 based on Access Economics (2008b) QALY value x Tariff x SLY	(129,519)	266,775	3,159,534	3,961,266	4,225,272	3,901,313	5,099,554	
Total	(130,454)	409,371	3,183,040	4,008,491	4,253,854	3,970,214	5,040,509	(11,526)
NPV at 0%	$20,723,498							
NPV at 3.5%	$17,384,641							
NPV at 5%	$16,164,529							
NPV at 10%	$12,812,638							
Analysis 2 based on PHARMAC expenditure per QALY								
QALY value ($6,900) x Tariff (0.92) x SLY	-$3,174	6,348	73,002	88,872	92,046	82,524	104,742	
Total	(4,109)	148,944	96,508	136,097	120,628	151,425	45,697	(11,526)
NPV at 0%	$683,664							
NPV at 3.5%	$592,630							
NPV at 5%	$558,703							
NPV at 10%	$463,271							

PHARMAC reports (2007 p 18)

> *Between the 1998 and 2005 financial years, new investments made by PHARMAC have cost around $6,900 per QALY (cumulative volume-weighted average). However, the cost-effectiveness of new investments has varied widely each year – reflecting both the mix of investment opportunities and the funding available at the time.*

Using a value for QALY of $6,900 produces an NPV of $592,630 at a discount rate of 3.5 percent. As in the higher range, analysis above the researcher perform an additional sensitivity analysis using a discount rate of 0 percent, 5 percent and 10 percent which creates a range of net benefits between $463,271 and $683,664. This reflects a smaller value than that calculated in the first analysis.

CONCLUSION

Benefit cost analysis (BCA) in the economic outcomes strand has little or no meaning without specifying a focal stakeholder that receives the benefit or bears the cost. This chapter presents the analysis for the economic outcomes strand from three perspectives by adapting a spreadsheet-based multiple account approach (Campbell and Brown 2003). The three sections of the spreadsheet reflect BCAs from different but related perspectives, namely: (1) the CCRep research unit (micro-level); (2) the CMDHB (meso-level); and (3) New Zealand society (macro-level)It presents the economic benefits and costs of two sponsored clinical trials conducted in a publicly funded New Zealand hospital over a period of eight years. The researcher finds that CCRep, CMDHB and New Zealand society all derive economic benefits from these trials.

The magnitude of the economic benefits differs depending on the perspective taken. CCRep has benefits ranging from $613 and $1,102 per participant. CCRep is able to reinvest this surplus into other research projects. This is greater than those of CMDHB are. Many participants maintain their enrolment in CCM at a continuing cost to the DHB. There are a number of reasons why this may be the case. The participant's general practitioner may have been unwilling to unenrol the participant and therefore lose the treatment subsidy or the patient may have needed to attend their general practitioner for other reasons. Despite suggestions from pharmaceutical company, representatives that health board's benefit greatly from treatment cost avoidance (Murphy and Maguire 2011b, Watson 2006) the current study finds the benefits from the

perspective of CMDHB are positive $871.11 per trial participant over the eight year period. The study finds the largest but potentially the most controversial benefit is a benefit to New Zealand society of over 373,000 dollars.

The next chapter, chapter 6 reports the results of the multiple stakeholder perceptions strand of the study. The final chapter of the thesis, chapter 7, concludes the thesis.

6. QUALITATIVE RESULTS FROM THE MULTIPLE STAKEHOLDER PERCEPTIONS STRAND

The previous chapter reports the quantitative results from the economic outcomes strand of the study. This chapter reports the qualitative results of the multiple stakeholder perceptions strand of the study. The final chapter of the thesis, chapter 7, presents the final summary and the conclusions.

The multiple stakeholder perceptions strand of the study reported in this chapter investigates stakeholder perceptions about the benefits and costs of clinical trials. The chapter presents the dominant themes arising across the groups and then compares the perceptions across stakeholder groups. The perceptions, opinions, beliefs and attitudes collected in this strand of the study are subjective and because of the small sample, size may not be generalisable across wider populations however, they do provide insights into the views of informant groups.

THE RESEARCH INFORMANTS

To avoid confusion the current study refers to its human contributors as *informants* rather than *participants.* The term *participant* refers to those involved in the clinical trials. The researcher uses analytically based purposive selection in the multiple stakeholder perceptions strand of the research. Hoffman (2009 p7) explains this method

> *Purposive selection means that research settings, data from these settings and research participants are located with reference to theory that indicates the selection is likely to address or lead to data that can answer research questions. Using theoretical concepts to guide the selection of data from the beginning—at the design stage of research—is the first step to interpretive data analysis designed to generate analytical generalizations — to theory*.

Purposive selection involves deliberately seeking informants who can contribute to the subject area and allow for analytical generalisations. As analytical generalisations are very different from statistical generalisations, the multiple stakeholder perceptions strand of the study does not provide a statistically representative sample (Rice and Ezzy 2000, Yin 2002).

As discussed in chapter 3, the multiple stakeholder perceptions strand of the study purposely selects informants to represent the following stakeholder groups: (1) trial participants (2) the family, community and other caregivers, (3) staff, (4) members of the pharmaceutical industry, (5) DHBs (6) the New Zealand community, and finally (7) the international community. In total, the views of 113 informants are collected.

THE BENEFITS AND COSTS FOR TRIAL PARTICIPANTS

Stakeholders perceive the benefits to trial participants as (1) increased care and attention, (2) increased monitoring, (3) being able to give something in return for the health benefits received in the past, (3) health benefits, (4) feeling of contributing to the greater good, (5) being able to have a choice of treatment options, (6) hope, (7) reassurance and (8) education about their condition.

Stakeholders perceive costs to clinical trial participants as: (1) parking and travel costs, (2) time taken, (3) trial treatment that does not meet expectations, (4) adverse medical events, (5) feeling like a guinea pig (6) lack of continuity of treatment following the trial, (7) developing a dependence on their medication and (7) being part of the placebo group.

Trial participants perceive the increase in the care and attention that as the greatest benefit that they receive from being part of the clinical trial:

> *It was not just checking your blood pressure but also answering questions to see if your memory was fading and things like that. There was quite a bit more to it and she has the time to do it. She was allowed time and did not have to rush to fit in her next customer. I never ever felt rushed. There seemed to be no time restrictions. We were never kept waiting and there seemed to be no one waiting when we left* (trial participant 1).

Another trial participant compares her visits during the trial to those to her general practitioner:

> *Being in the trial I felt very special, very nurtured and not rushed whereas at the doctors you wait for half an hour in a crowded waiting room with sick people coughing all over you then run into the GP and he says 'why are you here' and you say 'I need some more pills' and then he rushes you out the door and you say as you go 'oh I haven't had a blood test for so many months' and he says 'next time'. You pay your money and off you go whereas this was like going for a massage. It was just lovely* (trial participant 2).

The bond that develops between trial participant and the staff is seen as beneficial. One trial participant describes how motivating it is to see the commitment of the research staff:

> *the great thing was you saw people around you who were so committed that it sort of brushed off on you and you got committed to try to keep yourself right. There were so many people who just seemed to be taking such a personal interest you know it was great* (trial participant 3).

Trial participants also view the extra monitoring as beneficial:

> *What I loved about it was you had everything done, you know, talk about a baseline. It is like going into the army and you never get that from your GP - you just get your pills and that's it* (trial participant 4).

Some trial participants have other illnesses picked up by the research nurse, which might not otherwise have been diagnosed in time to take appropriate action:

> *A few years ago, I went to see the research nurse in the middle of the day. I felt fine- it was a six- monthly trial appointment where they give you the full check-up. She does the ECG and I had a left frontal blockage, which had turned up over the last six months so the next thing I was in coronary care. In a trial you are being constantly monitored to make sure you are ok and I always thought that if something seemed to be going wrong with my health or with my drugs then I could ring up the research nurse and she would get on to the cardiologist if she did not know the answer and it would be taken care of and to me that's a huge advantage so that's the biggie to me* (trial participant 5).

Close monitoring provides a form of reassurance even when the exact purpose of the trial is not fully understood.

> *I had heard so many things about people being very ill with diabetes. It put the frighteners on me and that made me want to be good and do anything to make myself well. I was involved in a trial - I think they were sampling drugs or something. I was pleased I was in the trial because it meant I had someone monitoring me the whole time* (trial participant 6).

Trial participants value the opportunity to talk to the research nurse about their condition:

> *It gives you permission to talk about your ailments which you do not normally get to talk about - you know; who wants to hear an old lady talking about her health, but here is an*

> *audience just for you and you can talk about how crook you are until the cows come home* (trial participant 7).

Being on a trial also helps the diabetics on the trials keep to their diets '*It made me behave. It was like going to weight watchers'* (Trial participant 4). Other participants also find that being monitored also assists them to keep to their diets.

> *They controlled my diet by asking when my levels were up "what have you been up to? Have you had this or have you had that?" Then I would admit I had had a little bit of ice cream. It is amazing how it registers in your blood and the nurse picks it up. You can't cheat at all* (trial participant 1).

The responsibility of being on the trial also helps with conforming to diet requirements: *'You just behave automatically because you know if you misbehave you are stuffing something important up'* (trial participant). Motivators for trial enrolment vary between participants. One-trial participant volunteers as a means of giving something back in return for the health benefits he has received in the past.

> *For my first trial I felt that I was very lucky that I had actually lived following my heart attack and I felt a huge debt to society following open heart surgery which cost the tax payer many thousands of dollars and that I was lucky to survive it* (trial participant 8).

Others feel that it is a chance to help future generations. This is particularly true for those who have genetically based disabilities: '*first I thought I might benefit from it and then I thought some one's got to do it to help the next lot.'* Adverse reactions to trial medicines are regarded as a cost to trial participants by nearly all groups except the trial participants themselves. Trial participants in one focus group feel that having an adverse reaction is positive as it makes them feel as if they are doing something worthwhile and important. As one participant describes:

> *I was fine all the way through my trial until I had the adverse reaction where my potassium levels went up and that gave me a sense of achievement because I felt that they were gaining some sort of knowledge of what I was taking - so I felt that I was really participating then and not just being part of the trial with nothing happening -so when something did happen they were able to gain some knowledge and that knowledge all goes into the pot and helps give them their answers so I felt I was really achieving something* (trial participant 9).

Pharmaceutical representatives, CMDHB staff and politicians feel strongly that gaining access to new medicines is a strong motivator for participation in a trial. However, those enrolled in the trials for patients at risk of serious cardiovascular events feel the support is more important than the medication '*The medicine was only a substitute for what I was getting anyway'* (trial participant). Most trial participants feel that it is easy to get the medicines they needed from their family practitioner but getting ongoing support is much harder as their general practitioner does not have time to investigate them thoroughly. Trial participants value being given the choice of being able to participate in a trial and the resulting '*feeling of control over ones illness'*. Linked to this choice is hope as one caregiver to an HIV trial participant describes:

> *The critical benefit is hope. Typically, when you get to be part of an HIV trial, standard treatments have failed so the alternatives are maybe this will work or this will be the end for me. So, there is a very substantial benefit and that is going to have a placebo effect as well. There is a positive effect for the person's health. There is also the sub category there that they end up on the drug rather than the control and the drug has a positive clinical effect so that is an upside* (caregiver 1).

A research nurse views education and trial participants' increased awareness of the factors, which influence their condition as the main benefits to her trial participants:

> *Education and awareness are the two big advantages. We educate, educate and educate. We explain why we are doing everything. What benefits it is to them to keep on track. I give all my patients my home number and they never abuse it and whenever they get into strife or feel they are on a roller coaster they will give me a ring* (research nurse 1).

By far the most talked about cost or disadvantage to participants in undertaking the trial is car-parking including the distance between the car park and the trial centre. Many trial participants have to bring someone with them to escort them between the car park and the research centre.

> *Getting there was difficult sometimes but the difficulty was getting parking close to the nurses' home. I can't walk very far and that is the hardest part. They reimburse you for your parking. What they need to think about is not so much the parking but some way that you can ring a man who can take you from a to b. There are plenty of people who can drive but they can't walk when they get there. Even a golf cart would be good* (trial participant 7).

The time taken to participate in trials is seen as a minor sacrifice:

> *When I was working on my own I could come anytime but I did lose time off work and a couple of times it was a bit awkward but then it was worth the sacrifice - and it wasn't a big sacrifice anyhow but you just feel that you are helping in a way. You may have a slight disadvantage but it did not cost you in anyway* (trial participant 10).

Researchers suggest that being part of the placebo group is a disadvantage for trial participants, particularly when the active substance proves beneficial. Trial participants themselves have mixed reactions to finding that they are in the placebo group:

> *In my study I was not on the active drug but on the placebo and I understand a lot of people not on the active drug did not survive. I was one of the lucky ones. In my case it is rather significant that the cardiologist has now put me on the drug that has lowered my cholesterol as a result of the study* (trial participant 10).

Some participants experience placebo benefits:

> *I found out at the end of the trial I was on the placebo - now all the time during the trial I was taking this lovely pill. My blood pressure was coming down until it was absolutely gorgeous and I got the letter that said 'Thank you. You were taking the placebo' and the next time I went to the doctor my blood pressure was well up and I can't believe this; he had to put me on proper medication to bring it down. I just couldn't believe it. It was a hoot an absolute hoot. I think there is a lot in your head, which affects your body* (trial participant 7).

One politician and some participants describe the developing of an overdependence on medications as opposed to lifestyle changes as a side effect of successful clinical trial:.

> *It is a little bit of my mentality now with this new drug it drops my cholesterol level down so low I don't seem to be able to beat the drug so I don't worry about diet anymore* (trial participant 12).

Several academic researchers and one politician feel concern for the vulnerability of some groups in clinical trials:

> *The poor and Maori carry the most risk in drug trials. They are often marginalised and not given the same access to treatment as the rich. They risk becoming teaching and research fodder. They are vulnerable and often do not understand the consent process. They may therefore agree to take part in trials because they do not realise they will still get good treatment if they don't. People who are unwell are especially vulnerable. There*

> *is a danger that the only way people will be able to get good treatment is through a trial. It is important that people be given a real choice which includes treatment in their own communities outside of the hospital* (politician 1)

This however is a minority view with most informants recognising the value of drug trials and believing that ethics committees in New Zealand are doing a good job at ensuring a high standard of research practice. The benefits that trial participants experience are perhaps best illustrated by the over 50% who have already participated in more than one trial and the almost 100% who said they will happily join another trial. The one person who is unwilling to be involved in a trial again is unhappy with the medications he had received.

THE BENEFITS AND COSTS FOR FAMILIES AND CAREGIVERS

The researcher asks stakeholders to consider the costs and benefits to families and caregivers. The emerging themes include (1) support; (2) education about the trial participant's illness, (3) the family may adopt a healthier lifestyle and (4) a better quality of family life. As with the other stakeholder group's informants identify a number of costs including (1) anxieties about adverse events, (2) time and travel and (3) increased responsibilities.

Whereas most staff feel that the trial participants' families and caregivers experience the same benefits and costs as the trial participants themselves, some participants and caregivers perceive their experiences differently. One caregiver describes her experiences of having a dependent family member on the trial. She suggests that the costs to the support person are much higher than many people believe:

> *When you are sick or have a condition then you get quite focused on that condition. The question you focus on is 'what am I going to do about changing it?' Other things start to have a diminished importance - particularly while you are in hospital. For caregivers all this drug trial stuff is going on as well as all the other stuff that you normally have to squeeze into your day. I am not saying it is easy for participants only their focus is more narrowed. It is anticipated that the benefits are going to be greater than the costs in the long term. The reality particularly in the short-term may be quite different and different for each family* (caregiver 1).

Family members cite the main benefit for themselves as the support and reassurance:

> *When he had his bypass operation and it was time to leave hospital there was no follow-up - we were just discharged. So when he was asked to go on the trial we at least thought he would remain in the hospital system and get some support. It was reassuring being on the trial. It is nice to have that security there* (wife of trial participant 2).

Some trial participants see their trial as personal and do not disclose their involvement to their family. Many who share their experiences feel their families are more fearful of the trial than they are. Often the caregiver has not been present when the trial invitation is made and is only told about it later by the participant.

> *My wife was quite anxious about me going on the first trial - more anxious than me. She was most anxious when I first agreed to do it - it was more the unknown she had just gone through nearly loosing* (sic) *me anyway and then when she comes to visit I tell her I have put my hand up for a drug trial* (trial participant 8).

Some researchers question whether the trial participant's family and caregivers actually benefit at all. A typical response comes from one researcher:

> *Most people would come along with their spouse others would bring other family members. In some ways they did not benefit at all but those patients that always came with their spouse seemed more likely to do better because they were well supported. Particularly when someone has had a serious life event I think families are as scared or often more scared than the patient themselves and so the trials became a prop or support for them if you like. Their needs or wants were being catered for as well and they became better equipped to help their family member* (researcher 1).

If the trial brings improvements to the health of the trial participant, researchers recognise that this can have flow-on effects for family members:

> *If the participant is feeling much better they will be less dependent and easier to be with. I had one patient who had got too unwell to dance. His wife loved dancing. Following the trial the participant was once more able to resume this activity, which really improved the wife's quality of life as well* (researcher 2).

Researchers also consider that the inclusion of health and nutrition education as part of some trials is beneficial to the whole family:

> *Often trial participants will adopt a healthy eating and life style, making positive changes to their behaviour. This may mean that they influence their familys eating pattern and*

> *lifestyles for the better. So you may end up benefiting the patient's family as well as them* (research nurse 1).

THE BENEFITS AND COSTS TO CMDHB RESEARCHERS AND STAFF

The researcher explores the perceptions of stakeholders as to the benefits and costs of clinical trials to Counties Manukau District CMDHB researchers and staff. Generally researchers and staff feel enthusiastic about being involved with clinical trial. Researchers and staff perceptions of benefits are wide ranging and include (1) developing collaborative international relationships, (2) providing experience and educational opportunities, (3) improving job satisfaction and motivation, (4) giving hope for better treatment options for their patients, (4) giving better information on which to base treatment decisions, (5) allowing cross-subsidisation of their other research activity (6) publications and (7) career advancement. Some however express concerns over (1) increased workload and time commitments and (2) the loss of flexibility and independence. Costs identified by other stakeholder groups included the management of patient's unrealistic expectations and the disappointment if the trial drug is unsuccessful.

All stakeholder groups strongly articulate the benefit of boosting international and inter-sectoral collaboration. These collaborative relationships are also seen to assist skill development and experience, something researchers and staff regard as important: *Often the funding from the drug / treatment trails can fund conferences, education and other things* (CMDHB staff member). Trial participants also acknowledge the value of overseas experience:

> *The research nurses seem to be travelling around the world to conferences and will be gathering additional information not just that which is directly related to the study. This means they will have increased knowledge that they can use on their return* (trial participant 12).

Researchers and staff identify positive themes of increased motivation, esteem and satisfaction. One staff member reports the *'satisfaction of seeing hard- to-treat patient groups have access to new treatments'* while another talks about her *'increased enthusiasm following involvement with a trial'*. Researchers and staff also discuss the positive '*impact on recruitment and retention'*.

Researchers identify both short-and-long term effects. Researchers and health board staff can gain access to more data on which to base their decision-making, allowing outcomes of the trial to influence their future work processes and workloads:

> *Staff need evidence before they change their treatment methods. Without research evidence to change treatment procedures it is too easy for staff to say 'we have always done it this way and it works and why change?' Robust research provides the evidence as to why change may be necessary. During the trial there may be no benefits but in the long run it may make staff more efficient and effective, reduce patient hospital stays and decrease workloads. It allows staff to lift the game of what they are doing* (researcher 2).

They see the cross-subsidisation of other research as a major advantage to health-board researchers and staff and researchers. This may also flow on to cost avoidance for the CMDHB as one researcher explains '*money received can flow sideways to support non-sponsored research - which may in turn reveal more cost-effective solutions – for example heparin instead of enoxaparin in DVT...*' The cross-subsidisation may make an otherwise marginal research team viable with sponsorship '*funds assisting, developing or supporting the research teams' sustainability'* (researcher 3).

Researchers and staff report that it is common for trial participants to be recruited from all levels of CMDHB staff. '*There is a firsthand opportunity for staff or their families to take part in certain trials that may offer great hope to some'* (CMDHB staff member 1). This is backed up by the number of the survey informants who indicate they had been participants in trials while a staff member. Finally researchers and staff regard the benefits arising from research publications and subsequent career advancement as strong motivators for staff to be involved in clinical research. Informants from across all stakeholder groups mention time factors as an important cost to researchers and staff:

> *There is a lot of work involved. It is not as simple as seeing a patient taking their blood pressure and sending them off, for example. They have to record and complete all the paperwork* (pharmaceutical company CEO 1).

Researchers see balancing time commitments as a cost:

> *There is not enough time: being available 24/7 in case of adverse events mean my resources are being diverted away from doing normal clinical work* (researcher 4).

One researcher feels there was '*uncompensated input for example in the hours taken to answer initial enquiries - many of which never lead to anything*' Combined with this time commitment is the perceived loss of flexibility and independence – '*the nuisance factor'* was expressed by a small number of CMDHB staff, in addition '*A trial may require you to do things in a somewhat different way than you otherwise would'* (CMDHB staff member 2).

Participant and local community member informants think managing the unrealistic expectations of trial participants and the community is a cost to CMDHB staff members. Although not mentioned by any researchers some stakeholders think researchers may become de-motivated as a result of a clinical trial for example:

> *There can be a negative impact on staff moral when they have invested large amounts of energy to create a result, which might say this substance has an advantage and then subsequently that substance does not turn out to be funded* (PHARMAC representative 1).

While most politicians agree that trade-offs may need to be made in order to achieve the benefits of a clinical drug trial, one politician feels these tradeoffs may outweigh the benefits when considering staffing:

> *It does relate to staff working on clinical drug trials and this may not be the most efficient use of your team in terms of your health outcome goals* (politician2).

THE BENEFITS AND COSTS FOR PHARMACEUTICAL COMPANIES

On asking Informants to consider the costs and benefits of clinical trials to the pharmaceutical industry the following themes emerge: (1) optimisation of returns to shareholders by securing long-term revenue, (2) the marketing of the drug amongst staff and patients, (3) creating an image of a socially responsible, innovative and competitive organisation, (4) the gathering of valuable data for use in applications for drug funding, (5) the competitive advantages of conducting trials within New Zealand as opposed to other countries and (6) developing positive, collaborative relationships with medical teams.

Informants perceive that costs include (1) the direct costs of running the trial, (2) the risk of the cost of major adverse events and resulting loss of reputation and (3) the risk associated with competition in the marketplace. In addition, pharmaceutical companies see (4) the risk of their

medications not being accepted for funding within New Zealand. Informants from the pharmaceutical industry view New Zealand as having a competitive advantage over a number of other countries who undertake clinical research because it has high quality researchers and a good record for recruiting trial participants. A chief executive officer (CEO) of one pharmaceutical company praises New Zealand's research ability:

> *Some of our investigators are of a world-class standard. We do a lot of testing of respiratory function and some of the tests are not easy to do. The tests have to be done correctly to validate the results. One big study we did a year or so ago in which the patients were followed up for four years, some of the best paperwork was completed here in Auckland where for their accuracy in recording their results scored in the top 3 in the world of all the sites that did that work so we have gotten some excellent investigators here* (CEO of pharmaceutical company 2).

A pharmaceutical industry representative observes:

> *We have exceptionally good investigators in this country who are very keen. They recruit their patients well. In some studies the recruitment in New Zealand is better than Australia* (pharmaceutical industry representative 1).

Members of clinical research organisations (CROs) suggest other competitive advantages of completing trials in New Zealand. Some believe trials in New Zealand are more cost-effective because pass-through costs (i.e. indirect expenses related to the purchase of third party services required for the conduct of the study) are lower and time savings are considerable without sacrificing quality. Some report New Zealand's diverse ethnic sub-populations as useful for many trials. In addition, they view New Zealand as having 'a southern hemisphere advantage of reverse seasonality, boosting international recruitment and allowing pre-season trials relative to European and American countries' and 'many New Zealanders have not been exposed to the range of drug therapies available in other countries'. A clinical researcher suggests that New Zealand has a 'broad range of disease profiles, including diabetes, cardiovascular diseases, cancer, neurological and infectious diseases' that may be advantageous for some trials.

Stakeholder groups other than the pharmaceutical industry, PHARMAC and Medsafe express a common belief that New Zealand based clinical trials assist in the process of obtaining registration and subsidisation of new drugs in New Zealand. However, according to PHARMAC, the location of trials is not a consideration when it considers the allocation of funding:

> *There may be health benefits in conducting trials in New Zealand, but you could conduct that research anywhere, and that could be equally useful. There could be some genetic or environment factors which might be identified for the New Zealand population. If there is information about these factors then PHARMAC takes these into account, but there rarely is* (PHARMAC manager 1).

Medsafe's view is similar:

> *We very rarely see applications for Ministerial consent to market where clinical data from New Zealand is included. Where some New Zealand patients are included in a study, it tends to be as a very small part of a large multicentre international study. The New Zealand legislation does not require studies to be undertaken in New Zealand before an application can be submitted* (Medsafe manager 1).

PHARMAC is however; interested in information that highlights the benefits to Maori and Pacific peoples. This needed information is seldom presented to PHARMAC:

> *The needs of Maori and Pacific people are something that we are trying to address. We rarely get information on the risks and benefits of medicines as they relate to this group. There is more information on such things as the access of these groups to healthcare in general but nothing specific to medicines. Information on the outcomes for Maori and Polynesian groups would be very helpful for PHARMAC.* (PHARMAC manager 1)

Some informants regard the marketing function of clinical trials as important. They report that trials help to '*persuade the pen of the doctor prescribing*' (PHARMAC representative). One trial participant suggests '*If we do not have trials here PHARMAC is not going to be pressured to bring new drugs into the country*.' Others feel that in some cases '*having doctors get used to using a product before a launch is a primary purpose in the structure of the trial*' (PHARMAC representative). Closely related to the marketing function is the importance of good public relationships developed during drug trials.

> *One way that the pharmaceutical companies maintain their charm effects with the New Zealand public is by conducting drug trials in New Zealand and thereby achieving some trial access for drugs and so it has a significant public relations benefit. I would argue that that is the main benefit that they receive from running trials here* (politician 3).

Some informants describe the relationship developed with CMDHB staff as beneficial to the pharmaceutical industry. '*If a pharmaceutical company is supporting investigator led research,*

there are advantages to them such as allowing access to data and building their relationship with researchers'. This relationship may also lead to researcher endorsement of the pharmaceutical company's products '*They get to brand their product with the endorsement of research and research scientists and clinicians*' (researcher 5).

However, most pharmaceutical company representatives interviewed feel that New Zealand is a hostile environment in which to operate according to the

> *Many of the costs are only in New Zealand. In the very hostile environment we have for pharmaceuticals in this country what I mean is we do a clinical trial and clinical trials are not inexpensive to conduct. We gain all the data we need for submitting to Medsafe or the approving agency. We do all that and then we try to gain reimbursement so we can commercialise the product and bring it to market here. In a lot of cases we can't get reimbursement for those products like we can in most OECD countries. If we take Australia for example between 2000 and now there has been 84 new pharmaceuticals made available over there which are not available here because of our funding system. So the risk in New Zealand is the huge investment with no return, as we can't bring the products in* (pharmaceutical company CEO 2)

Pharmaceutical industry representatives also feel that fewer clinical trials are being conducted in New Zealand as a result of poor commercial returns in this country

> *There are a lot of companies that are not conducting clinical trials here now. There is some data available that compared expenditure on clinical trials in New Zealand. In the early 90's it was around $100 million and more recently between $18m and $20m. There are examples of clinical investigators who have had to move off shore because they can't get work here* (pharmaceutical company CEO 1).

Several managers of research units, Medsafe and PHARMAC representatives dispute this view; they feel that clinical research in New Zealand is increasing. They suggest that although the pharmaceutical industry is not directly conducting clinical trials in New Zealand they contract with clinical research organisations (CROs) to manage trials on their behalf. The pharmaceutical industry has suggestions to improve the environment in New Zealand:

> *To improve the conditions here, firstly there should be greater transparency in the process. That is the big one. Our authority is like no other in the world. In the United Kingdom, the National Institute for Clinical Excellence (NICE) committee allows*

> *pharmaceutical companies to appear before the committee and present our case. The Food and Drug Administration (FDA) is the same thing, whereas here we submit an application and we hear very little about it. We don't know what goes on behind the scenes, we simply get a recommendation, but we don't know what's behind it and what the recommendation means; as an example, PHARMAC may recommend that the product be reimbursed with a high medium or low priority. There is no transparency around what those priorities mean. Another thing that will improve the situation is for the government to separate assessment and procurement so that these processes are not conducted by the one organisation* (pharmaceutical company CEO 3)

Only politician interviewed thinks PHARMAC needs to adjust its approach. The rest regard PHARMAC's performance as excellent, with one politician going so far as to say, '*It is the only government department that is working well*'. Many describe the pharmaceutical marketplace as highly competitive, which can result in a company paying for a trial only to be beaten to the market by another company. Some informants observe that as many of the differences between drugs are relatively small, it is difficult for pharmaceutical companies to make a convincing case for PHARMAC to adopt their product:

> *The industry is pretty competitive these days especially in diabetes medication. What the drug companies say to us is - "you are not doing any comparable study are you?" They do not like one site doing say more than one trial on any one type of drug over the same time period* (researcher 6).

Informants from some stakeholder groups consider the risk of major adverse events a cost to the pharmaceutical industry. The pharmaceutical company representatives, however feel adverse reactions are rare:

> *There was a case a couple of years ago where there was a problem in England with a phase 1 trial. In phase 1 we are still learning about the drugs. These events are few and far between. There is a risk however with any medical intervention. There are always risks of adverse events* (pharmaceutical company CEO 1).

Informants feel that the pharmaceutical industry is also at risk of damaging their reputation from adverse events that are unrelated to the trial:

> *If there was an adverse event family members often were attributing this to the medication and the trial. It became an easy thing to blame even if it was not the trial medication at fault* (researcher 7).

Although trial participants are aware of adverse events that have occurred in other countries, most felt that New Zealand trials are much safer. As one member of a focus group said: '*Clinical trials are quite safe in New Zealand. We haven't had anyone wake up with their toes fallen off have we?'*

THE BENEFITS AND COSTS FOR THE DHB

Elected CMDHB members are supportive of sponsored clinical trials within their hospitals although they view research as playing only a minor role in their overall responsibilities. There is also general agreement among politicians, CMDHB staff members and researchers that CMDHB benefits from allowing sponsored clinical trial to be conducted on site. Themes to emerge included enabling (1) the development of sound medical practice guidelines, (2) a choice in treatment options, (3) research into local diseases, (4) treatment cost avoidance, (5) cross subsidisation of other research activity, (6) greater status and reputation and (7) improved staff recruitment and retention. The perceived costs are: (1) having to provide the infrastructure required for trials, (2) the opportunity cost in terms of staffing and other resources, (3) the risk of major adverse medical events, (4) the risk of distraction from core business and finally (5) the risk of becoming dependent on sponsor funding.

Clinical trials provide the evidence needed to develop practice guidelines. As explained by a CMDHB staff member '*Understanding of Good Practice guidelines and 'cutting edge' treatments increases patient safety and levels of care provided* '. Some see sponsored clinical trials as reducing costs for CMDHB while at the same time providing clinical and research resources, which they might not otherwise have access to. '*Clinical drug trails can be a source of revenue for the District CMDHB; this can then be used to support in-house research*' (CMDHB staff member 3). The in-house research may also result in additional benefits. One researcher described a direct saving as a result of a cross-subsidised clinical trial:

> *Some trials have led to better treatment, for example, the trial involving the temperature of saline solutions on wounds. We took days off wound healing because of this so it was*

> *win win all around and it would never have happened without clinical trials (researcher 2).*

CMDHB Staff believe CMDHB can attract clinical trials in areas that they target as priority diseases. One researcher suggests that sponsored clinical trials are a way for CMDHB to manage their most difficult diabetes patient – the ones whose diabetes has proved most challenging to manage:

> *We get the most difficult patients and generally find solutions for them. The inclusion criteria for getting into most of my trials is poorly controlled diabetes. They often have things like cardiovascular disease that they also want in the trial* (researcher 1).

Cost avoidance can occur as a result of sponsored clinical research centres by removing patients out of the public system for the duration of the trial. This has the potential of providing significant CMDHB cost avoidance. As one politician observes:

> *Quite significantly, patients are seen by people other than routine staff. Often those people are employed by the Boards but the treatment regimes and the pharmaceuticals themselves are provided by the drug company and so that is a direct saving to the District Health Board. District Health Boards should be encouraged to do more trials. I think it adds another dimension to the services that a Health Board offers* (politician 4).

Politicians also view advantages in the increased status of DHBs engaged in clinical trials.

> *There is a benefit around the perception of the Board being innovative and it therefore produces political and clinical leverage, which is useful* (politician 5).

This leverage also manifests itself in the CMDHB's ability to recruit and maintain staff, which they believe, improves the quality of treatment:

> *A District Hospital will never be a centre of excellence if it is not conducting research. Doing quality research and being a centre of excellence lifts the profile of the hospital and attracts the very best staff* (researcher 7).

They suggest that long-term benefits can be achieved from successful clinical research:

> *The success of clinical trials has a major impact on future funding. If a drug or treatment is found to be more successful than standard treatment it can lead in the long term to huge reductions in the cost of care* (researcher 8).

Members of the pharmaceutical industry identify considerable benefits to CMDHB as a result of clinical trial being conducted on site:

> *They are producing revenue from the trials they conduct. Their scientific staff are exposed to international best practice. Having a clinical trials unit assists with staff recruitment. It will help them attract some of the best brains in the world. This goes through the chain and benefits everybody* (pharmaceutical industry representative 3).

Industry representatives explain that District CMDHBs and private research units actively seek opportunities to conduct clinical trials. One company representative describes the selection process:

> *We select on history and recommendations from other parties. We send our people along to look at their systems and conduct an assessment of their abilities* (pharmaceutical industry representative 4).

Some CMDHB staff indicate concern that clinical trials put '*Pressure on available space with office and clinic space required for trials*' While one CMDHB employee feels that clinical trials are an *'Inappropriate use of facilities'* others are supportive of the need for CMDHB to ensure it has '*good support and infrastructure to enable clinical trials to be conducted'* (CMDHB staff member 4).

Concern over the sponsorship of clinical trials is raised by a small number of survey informants who feel uneasy about the close relationship between sponsors and medical staff. One CMDHB staff member feels sponsored trials

> *.....take the place of research into questions worth asking. It represents an overall dummying-down of 'academic' research in New Zealand. The research empire that has grown locally at CMDHB has deliberately prevented other research from being conducted here - it has REQUIRED all research to be channelled through it - and it refuses to undertake research that does not show a profit. Some staff are paid bonuses based on how much revenue is generated. Basically, research becomes not an academic investigation but a revenue gathering / empire building exercise. Furthermore it encourages sponsored research into New Zealand where we might be better doing basic science - something New Zealanders have historically done well, but nowadays New Zealanders usually do much better by going overseas!* (CMDHB staff member and researcher 5).

A few express anxieties over the purpose of some sponsored trials and the way they are conducted. A clinical researcher observes:

> *Some trials seem to be simply marketing tools to encourage use of product in different indications, whereas others seem to be genuinely exploring effects (for example adjuvant cancer therapies) that might not otherwise be available* (researcher 6).

Many informants talk about research that has gone wrong in the past either in terms of adverse events or ethical standards. They express concerns that the CMDHB may be implicated if similar events occur at CMDHB. Some refer to the Cervical Cancer research study at National Woman's Hospital known as the 'unfortunate experiment'. The National Woman's Hospital study[4] has had a major impact on the way that health research is conducted in New Zealand as is explained by one CMDHB member:

> *The unfortunate experiment is never going to go away. It will be a very tender issue in our society. Forty years afterwards there are still aftershocks. Yes it is huge. If something goes terribly wrong. It is a very very serious thing. We must do research with the very best quality and standards - that is all we can do. If something goes wrong the costs are going to be much much greater. The people or participants involved the researchers whose reputations are ruined CMDHB and the sponsors have costs associated with trials that go wrong. People are still trying to find answers about what went wrong in the unfortunate experiment* (elected member of CMDHB).

Researchers perceive that some trials as not cost effective. There is some variation in the fees earned for running a trial and the same trial may have different cost and payment structures depending on where it is run and what negotiations take place. Whereas some research units take without question what the pharmaceutical company is willing to offer to run a trial, others are strong negotiators. Some units have a greater awareness of the costs associated with trials than others and use this information to make decisions about which trials to undertake.

> *Sometimes we turn projects down on a cost analysis – some of the pharmaceutical companies now do not pay enough for the time that the staff will put into the patients and the number of visits and so the costs start to come into it* (researcher 9).

[4] This study which began in 1966 was designed to demonstrate that a symptonless lesion of the cervix, carcinoma in situ, would not lead to cancer (Coney, 1988). An on-going observation of the lesion occurred but no treatment was given which resulted in severe illness and fatalities in Several woman (Hudson, 2004). The woman were not informed they were part of a research study and therefore had no opportunity to give their consent.

However, one politician has concern about the sustainability of revenue gained as a result of CMDHBs undertaking clinical trials and that boards that become dependent on gaining revenue in this way may be at risk if the funds are to suddenly stop. They conclude their interview with the warning:

> *We must be cautious in engaging in these trials. We need to be cautious about becoming dependent on research funds as a source of revenue for DHBs* (politician 1).

As explained in chapter 3 this thesis adopts the world view that the quantitative results (economic outcomes strand) described in chapter 5 and the qualitative results (the multiple stakeholder perceptions strand) described in chapter 6 are complementary. Each strand delivers dimensions to the analysis that are not apparent from the other. The data are complementary in the sense that they produce a collage capable of delivering an understanding of clinical trials in New Zealand; however, the data are not amenable to producing a meaningful composite. As data relating to many aspects of the study can be obtained via only one of the available research methods, the researcher's view is that quantitative and qualitative methods can be combined in the current study only for complementary purposes. Given that researcher had a strong sense from the inception of the project that a quantitative analysis on its own would lack balance, she seeks complementarity through a mixed methods approach. Richardson (2000, p. 14) prefers the term 'crystallization' to 'triangulation' to compare data sources and highlight complementarity. She chooses a crystal rather than a triangle to represent the relationship between data sources because a crystal has multiple surfaces. It is able to reflect and refract and therefore create multiple images of reality. Whereas the triangle suggests there is one single triangulated truth, the crystal symbolises the possibility of multiple truths (Janesick 2000).This is consistent with Sale et al. (2002, p. 43):

> *. . . the paradigms upon which the methods are based have a different view of reality and therefore a different view of the phenomenon under study. Because the two paradigms do not study the same phenomena, quantitative and qualitative methods cannot be combined for cross-validation or triangulation purposes. However, they can be combined for complementary purposes.*

However, the researcher observes some minor overlaps when compiling the two sets of results. First, the quantitative analysis in chapter 4 supports the stakeholder perception that CMDHB

gains revenue from conducting clinical trials. CCRep uses some of this revenue to offset additional research that takes place within the DHB. The perception that participants enrolled in clinical trials are 'removed' from the normal hospital system gains partial support from the economic data presented in chapter 5. The economic data also provide partial support for the perception of savings from pharmaceutical cost avoidance. Cost avoidance occurs for three years during the trial, however this is reversed at the end of the trial. This may have been due to the participant having to have their medicines adjusted after the trial particularly when trial medicines are not readily available. The economic data supports the perception of cost savings from laboratory testing. Although the financial gains the study identifies in chapter 5 are much smaller than many in the qualitative study perceive, they do support stakeholder perceptions that conducting clinical trials provide financial benefits for CMDHB.

THE BENEFITS AND COSTS FOR THE NEW ZEALAND COMMUNITY

The researcher asks informants for their perceptions of the costs and benefits of clinical trials to the New Zealand Community. Perceived benefits include (1) the economic benefits associated with overseas sponsors investing in New Zealand, (2) the cost avoidance in terms of sponsored participant treatments and (3) the development of medicines tested for New Zealand conditions. Informants recognise opportunity costs in terms of (1) research resources and (2) non-pharmaceutical treatments. A common theme emerging across all groups relates to the economic benefit of running trials in New Zealand. This includes informants associated with oversees sponsors investing in New Zealand-based clinical trials and cost avoidance achieved by removing trial participants from the government funded health care system. Informants also think that clinical trials enhance New Zealand's profile and thus increase the likelihood of further investment within New Zealand. *Participation in international drug trials increases the profile of New Zealand as a venue for research, bringing in international finance and recognition* (CMDHB staff member)

Trial participants, their families, CMDHB staff members and some researchers perceive that conducting clinical trials in New Zealand provides the assurance that the new drugs have been tested on New Zealanders and are therefore safe for use by New Zealanders. In addition they feel that environmental factors and diet may influence the way New Zealanders react to drugs.

Medsafe has a different view and does not take into account genetic or diet factors when considering the safety of medicines though this may change as more information becomes available:

> *As we get more information about pharmacogenetics, i.e. whether genetic subtypes influence medicines' efficacy it may become clearer that certain members of the New Zealand community do respond to different medicines differently, e.g. Pacific Island peoples or Asians may metabolise different medicines in a clinically significant way, however, at this point in time, we do not really see any significant examples of this occurring in the information we have available to us* (Medsafe manager).

Informants from all groups think that the conduct of trials in New Zealand provides opportunities to address local health issues:

> *I was on a six- month selenium trial that was directly related to New Zealand, as New Zealand's selenium levels are very low. There was no point doing that trial in Australia or somewhere else where the selenium levels were already high* (trial participant 13).

In particular, some trial participants feel that their trial is very important to the future health of New Zealanders:

> *Citizens of New Zealand moving forward will have a better chance of survival than I will have because of my drug trial and the drugs it has introduced* (trial participant 14).

The main perceived cost is the displacement of other health care activities. As one informant commented:

> *I would wonder whether this type of activity displaces other activities. If it displaces more beneficial activity then the health status of people in Counties Manukau and other parts of New Zealand are disadvantaged*. (PHARMAC manager)

Some members of the community are not aware that clinical trials are being conducted in New Zealand.

The perceive financial benefits from the revenue gained from conducting overseas sponsored trials and also from a healthier population are supported by the evidence produced in the two trials reported in chapter 4.

THE BENEFITS AND COSTS FOR THE INTERNATIONAL COMMUNITY

Although we did not specifically seek informants to represent the international community the initial sections of the questionnaire given to other stakeholder informants explores perceptions of the relative benefits and costs of clinical trials to the international community. There are no discernible differences between stakeholder groups in their perceptions of benefits to the international community. The common themes relate to (1) improvements in world health, (2) benefits associated with all countries collaborating for a common cause and (3) gathering data on new medications using a wide population base is seen as beneficial. Informants suggest this data will aid future decision making particularly in the allocation of health spending.

Some CMDHB staff members express concerns about the cost of clinical trials to the international community. Emerging themes include (1) the opportunity cost in terms of research resources, (2) the opportunity cost in terms of non-pharmaceutical treatments and (3) the increased cost of medicines.

Informants regard clinical trials as an important step in the introduction of safe new medicines and the elimination of world diseases. They see the increased life spans within the world's population as a direct result of clinical trials.

> *My elderly parents had extended life spans because of drug trials, which meant they had medications that were suited to their needs. They lived much longer than their parents* (politician 6).

Informants frequently mention the arguments concerning the importance of medicines for combating disease. Many, particularly elderly trial participants, recall serious diseases that inflicted people within their lifetime, but have since been eliminated by vaccines or other medications.

> *If we go back to when I was a lad we had polio - we had to close the school for three months. We don't have polio today as we did in those days* (trial participant 15).

Many informants across all stakeholder groups feel that New Zealand drug trials are part of a global approach to meeting patient needs and that New Zealand is doing its bit to help with world health goals:

> *We can put our hands up and say we are good international citizens because we are contributing to our share of international research and development of new medicines* (pharmaceutical company member 1).

This comment reflects the view that trials are for the greater good of humanity. A minority view is that New Zealanders are benefiting at the expense of other countries:

> *The rest of the world takes the risks for New Zealand particularly when conducting phase 1 trials, which we do not do a lot of. It is in these early trials that the risks are less known* (researcher 1).

PHARMAC highlights clinical trials as a major benefit in that they provide information on the efficacy of the drugs being tested. Health care systems internationally are being challenged with the growing costs and demand of medicines. Governments and other payers need to decide how much they can afford to invest in medicines and then they must develop a process to decide the best value for the money spent. Informants perceive that clinical trials are a means of obtaining efficacy data to achieve this objective. One PHARMAC manager (a government official) commented thus:

> *We are fortunate in the pharmaceutical area in decision making because the information generally is pretty good in comparison with a lot of other sections of the health sector, which would not have as complete information or knowledge basis that we have* (PHARMAC manager).

Nonetheless, although many informants regard robust research data as desirable, they express concern that this must be balanced with strong ethical practice because of clinical trial data is sensitive. Some informants regard overt information sharing as important for good decision making within the health service and they believe that negative results that are not shared can have far-reaching consequences.

Many informants, mainly politicians and CMDHB staff members show their mistrust of pharmaceutical companies who appear to put their profit making goals ahead of patients' needs. Many researchers, CMDHB staff and politicians emphasise the importance of strong ethics; however, they disagree about the ethical standards applied in recent clinical trials. Examples of unethical behaviour include reporting the results of trials favourably and taking advantage of the sick and vulnerable. Some informants also suggest that the relationship between the funder and

researcher is too close. '*Trials are viewed as potentially biased because they have been funded by the company*' (researcher 8).

Informants' responses show concern about the opportunity cost of clinical trials in terms of research resources consumed. This includes using resources that might otherwise have been used to investigate diseases of the poor or non-pharmaceutical treatment options. Only a few politicians and some CMDHB staff members hold these views, for example:

> *Drug companies treat diseases that are lucrative to treat, for example, we still have malaria as one of the world's major health issues, but it is not addressed because resources are channelled to the rich - who don't get malaria* (CMDHB staff member 3).

However, some politicians recognise that drug trials are provide treatment options for people in poor countries that may not otherwise have other treatment options available to them and that many poor countries are now lifting their gross domestic product by producing generic medications.

> *Equity issues with regard to access to medicines are a long running debate. Pharmaceutical companies have to develop the drugs before anyone can benefit but what we are seeing is generic drugs being produced, often in the poorer countries such as India and China, which will benefit those countries sometimes at the expense of the large pharmaceutical companies that originally developed the drug* (politician7).

Examples of good, ethical practice occurring with contemporary trials include robust ethics approvals processes, open label inclusion (ie, doctors and participants know which drug is being administered) and prolonged control group treatment. One focus group of mostly elderly trial participants worries that young people today too readily discount the value of medicines. A similar view is that medicines are too often used as a quick-fix solution to complex medical issues. The following three quotes regarding over-reliance on medicines reflect the perceptions of different stakeholders:

> *We should focus on the potential of people to navigate their own journeys. Communities should be given the ability to find their own solutions. Unfortunately, placing too much emphasis on pharmaceutical medications can provide a reliance on quick-fix solutions without tackling the root of the cause. We need to focus on strategies that bring about a change in attitude and behaviour about leading healthy lives* (politician 8).

> *Attention is focused on pharmacological solutions instead of prevention, supportive care, and basic health measures. Often advantages for new treatments are slight and may not be sustained - these drain money away from other more relevant health interventions* (CMDHB staff member 3).
>
> *Sometimes I wonder if we have gotten too dependent on medications One of my grouches about the medical fraternity is when things go wrong one thing they seem to do is keep on adding the drugs - they never want to take any off!* (trial participant 14).

Another politician expresses concern about clinical trials being too short:

> *There are incentives for drug companies to take their drugs to market before they have been fully tested. Why hold up profits testing a drug when it can be "tested" on first users--the public--and make money at the same time?* (politician 8).

Others feel that long clinical trials tend to increase the costs of medicines: '*New expensive drugs are driving up the cost of health; new drugs are replacing older cheaper drugs with limited evidence of improvement*' (politician) and '*expensive clinical trials drive up these costs further*' (academic researcher). One focus group consisting of mainly elderly trial participants recalls haunting images of children born with defective limbs. This occurred after pregnant women took Thalidomide for morning sickness. Thalidomide had been tested on rodents but not on humans (Monamy 2000). Members of this focus group consequently held the view that any costs involved in trialing medicines before the general population uses them are justified, for example:

> *I went through the time of Thalidomide. That was in very common use when we were having our first child and we were lucky my wife did not take it. I don't think they tested that drug properly and as far as I am concerned the more they test a drug before it goes on the market the better* (trial participant 16).

EMERGING THEMES

The qualitative descriptive approach used in this chapter allows the stakeholders to express their perceptions and stories in their own words and therefore stays close to the transcribed data in reporting the findings. This chapter uses many citations and describes the informants' experiences in a language similar to their own, which produces considerable rich data. However,

some key themes worthy of special mention emerge because of this analysis and are discussed next.

The clinical research community in New Zealand is small. One key source of value stakeholders identify is from the relationships, which clinical trials facilitate. Working locally and internationally with other like-minded people is important to researchers. The long-term nature of many trials results in the development of strong bonds that are valued by staff, participants and participant families. This strong feeling of camaraderie has a positive influence on retention within the research workforce and is regarded by some as compensation for the often-heavy workloads associated with their research role. Participants, particularly the less mobile who lived alone value regular contact with the research nurse and express regret when the trial ends. The exchange of small gifts at Christmas and some regard the research nurse as "almost family". The trust that develops between the participant and research staff means participants feel able to ask questions that they may not otherwise ask and share their experiences more willingly. Informants view trust in the New Zealand health system as important for the successful recruitment of participant volunteers. As identified in the quantitative results of this study recruitment is an important trial cost driver. With trust comes the responsibility to act in a way that warrants the trust given.

Reputation is often identified as both a cost and a benefit across stakeholder groups. Clinical trials can influence the reputation of all stakeholder groups. The reputations of New Zealanders, pharmaceutical companies, the health board and researchers can be enhanced when trials are successful, however at the other extreme if trials go wrong then the reputation of all involved can be damaged. Having a good reputation brings additional benefits. It attracts funding to the health board, attracts additional research sponsorship, enhances recruitment and retention of staff and builds moral. Pharmaceutical companies enhance their legitimacy through successful trials. The sense of pride associated with a successful trial extended to the participant and to family members. They saw the risk of ruined reputations as a potential cost of clinical trials.

Informants note that unethical behaviour or severe adverse events damage reputations. . Informants often cited National Woman's Hospital as a hospital that has suffered considerably following unethical behaviour during the "unfortunate experiments" discussed earlier in this chapter. Informants also viewed pharmaceutical companies as being most at risk of acting in an unethical manner but they also considered the conduct of the researchers themselves as risky.

The need for strong ethics committees to review all research was emphasised as key to promoting ethical behaviour. While ethical committees are viewed as critical to ensuring good conduct within clinical trials, they are also viewed as a cost. Tedious repetitive ethics forms, delays in the process of obtaining initial approval, having to consult ethics committees over minor protocol changes, reporting adverse events and inconsistency across committees were all seen as adding to the cost of a trial. While no one suggests ethics committees are not needed, a review of the ethics approval process may be warranted.

Another key theme to emerge from the research was the concept of hope. Hope on behalf of the pharmaceutical company that they may have discovered a valuable cure, hope on behalf of the researcher physicians that patients in the future will have better treatment choices, hope from the participants and their families that their participants illness may be cured. Some family members describe the trial as "*a light at the end of the tunnel*". While hope was generally seen as a benefit, there is some concern that false hope may be a cost. Often the participants do not experience the benefits of the themselves; the trial may benefit only future patients, as the treatment needs further refining. If a participant has a false hope for an illness that cannot be cured, then it may interfere with the acceptance process and rob valuable time from participants. Giving false is described as unethical.

Not surprisingly for a research activity learning, education and training was a major theme to emerge in this study. Again, more than one stakeholder group shared this benefit. . Pharmaceutical companies learn from working with practitioners in the field. They also learn from the real life experiences of the participants. They are able to use this knowledge to improve treatments. Researchers and staff learn more about the illness and treatments they research. PHARMAC learns about the effectiveness of the treatment under study. The participants and their families learn more about their illness and how this can be managed.

Chapter 5 of follows PHARMAC's advice to exclude 'indirect costs to patients' has been followed (p. 130). Therefore indirect costs to patients are considered as part of the qualitative analysis. Responses are analysed for inclusion of any indirect cost to patients and are discussed in the interviews and focus groups. As expected politicians, researchers, staff and pharmaceutical companies identify indirect costs to patients as including items such as time off work, transport, parking and childcare. Although accountants and economists might view these items as costs, in general the trial participants do not. They feel that this expense would have occurred anyway had

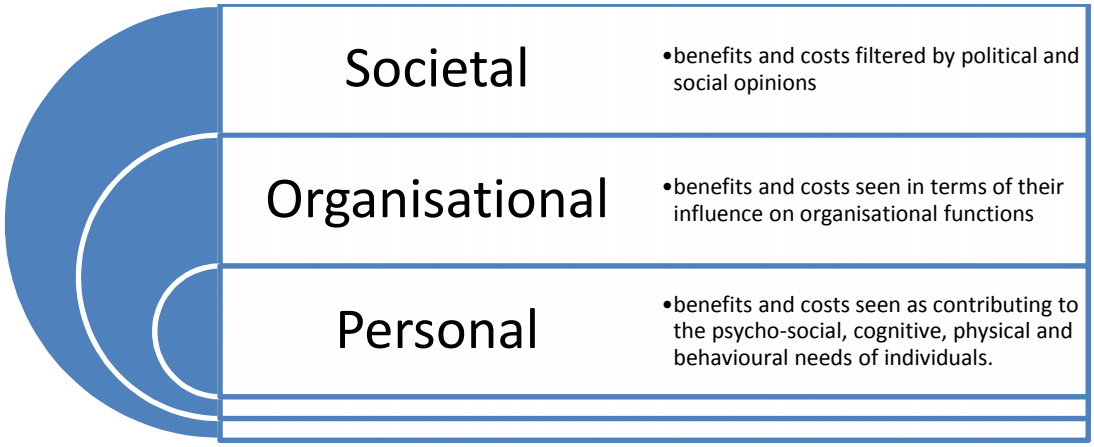
they received treatment at the hospital or their general practitioner. They are offered parking refunds, but many do not take them because they view the research as valuable and they do not want to take any money that might otherwise be used for advancing important treatments. Participants say they are given considerable flexibility in appointment times so are able to attend at a time that is most convenient to them. This along with not having to wait for long periods in general practitioner's waiting rooms means the research appointments are regarded as more preferable to other types of treatment available. Although participants acknowledge that, they need to attend appointments more frequently, most view this as a benefit rather than a cost as they feel that any worsening of their condition will be detected earlier.

PHENOMENOGRAPHICAL ANALYSIS

As described in chapter 4, this study uses phenomenography to analyse the stakeholder's perceptions of the benefits and costs of clinical trials. This approach assumes that the informants vary in the way they perceive the benefits and costs of clinical trials and that these perceptions will govern their subsequent behaviour (Marton 1986). The analysis produces a layered model of the phenomenon, achieved through collecting individual perceptions and then describing variations (Baker 2001). Conceptions are categories of description, which represent the collective understanding of the phenomenon (Barnard, McCosker and Gerber 1999). The informant perceptions of clinical trials condense into three layers of conceptions (1) societal (2) organisational and (3) personal (figure 6.2). The conceptions represent the ways stakeholders experience, conceptualise and understand clinical trials. As described previously the researcher uses NVivo 8 to assist this process.

Informants represented in each of the layers identify costs and benefits in different ways from those in the other layers. The layers have characteristics that represent the central meaning of conceptions.

FIGURE 6-1 UNDERSTANDING THE BENEFITS AND COSTS OF CLINICAL TRIALS.



Within the societal layer, perceptions of the benefits and costs of clinical trials are filtered by the informants' political and social opinions particularly their views on free market policies versus government regulation and their attitudes towards libertarianism and egalitarianism (as discussed in chapter 2). Within the organisational layer, informants perceive the benefits and costs of clinical trials in terms of their influence on organisational functions finance, human resources, operations, marketing and public relations and knowledge management. Within the personal layer informants, perceive benefits and costs as contributing to the psychosocial, cognitive, physical and behavioural needs of individuals.

The three layers of conceptions reflect the qualitatively different ways the benefits and costs of clinical trials can be described, analysed, and understood - something Barnard *et al.*,(1999 p212) view as important,

> *It follows that in health care research, it is essential to recognize the qualitatively different ways phenomena are experienced and understood. Recognition can have an important impact on health care, health maintenance, clinical practice, theory, and education. Central to improving health care and developing any discipline is identifying the ways in which phenomena are understood and experienced by practitioners, patients, institutions, and society.*

In this study, as in other phenomenographic research (see for example Anden *et* al. 2005 and Marton 1981), the three layers of conceptions represent the collective understanding of the phenomenon. The conception within each layer cannot be attributed to any one informant, and

each informant may perceive more than one conception (Barnard *et al.* 1999). The relationship between the conceptions is represented by the outcomes space. *The outcome space is a diagrammatic representation of the logical relationships between conceptions* (Barnard *et al.* 1999 p220). In phenomenographic research the outcomes space may depict conceptions as equal in value or as having a hierarchical value (Marton 1994). The outcome space in this study is hierarchical because although each of the three layers is a unique conception, they are integrated in a hierarchy of three incremental layers of understanding, ranging from the widest (societal) to the narrowest (personal).

Analysing the perceived benefits and costs of clinical trials by moving up and down these layers helps focus attention more effectively than simply considering one layer alone. The New Zealand Parliament Health Select Committee enquiry into improving New Zealand's environment to support innovation through clinical trials (The New Zealand Parliament Health Select Committee 2011) provides an example of this. This report is based on a societal view that private public partnerships are good for society (a free market perspective). If a different perspective had been taken the report would be very different and may not have been written at all. The report separates benefits at the organisational level (for example human resource benefits in the form of attracting staff) from those at the personal level (for example benefits for patients). Together these layers provide an effective, deep, and inclusive, report of the benefits of clinical trials.

The focus of the study is on the different ways of experiencing clinical trials. This is called a second order perspective and it is different from a first order perspective, which describes things as they are Marton (1981). Although not fully overlapping there are close links between the layers in the phenomenographic analysis and the macro, meso and micro-levels in the economic outcomes study. Both of these approaches produce a system of incremental layers of understanding, ranging from the widest to the narrowest. However, as discussed in chapter 4 there are key differences between the strands. The phenomenon in the economic outcomes strand of this study is '*the benefits and costs of clinical trials'*. In the multiple stakeholder perceptions outcomes strand the phenomenon itself is not the focus; rather the study focuses on how individuals '*perceive*' the benefits and costs of clinical trials.

PERCEPTIONS ACROSS THE STAKEHOLDER GROUPS.

This study provides an understanding of the variable perceptions of clinical trials both between and within stakeholder groups. As observed by Quintiles (2011 p8) *the constellation of stakeholders within the healthcare universe is intricately linked yet often misaligned*. There is consensus across the stakeholders on some benefits such as giving 'hope' and 'choice' to participants, developing safe medicines and collecting useful data. Perceptions differ markedly in other areas, as indicated below.

While most stakeholders perceive the risk of adverse reactions as the greatest cost to trial participants, the participants themselves do not regard this as significant. Pharmaceutical representatives, management and the multidisciplinary team feel that gaining access to new medicines motivates people to participate in a trial. Trial participants feel that the support is more important to them than the medication. While most researchers and staff believe that their involvement in trials increases their job satisfaction, motivation, knowledge and skills, a few have concerns that sponsor control leads to the loss of their flexibility and independence. There is a general perception that New Zealand-based clinical trials assist in the process of obtaining registration and subsidisation of new drugs in New Zealand. However, this perception may be erroneous, as pharmaceutical companies apparently do not consider the location of trials is in the drug registration process.

Many informants across stakeholder groups are concerned that the opportunity cost of running clinical trials at Middlemore may mean that the buildings and facilities used for trial purposes cannot be utilised for other clinical purposes. CCRep is housed in a building known as the 'Support building' located towards the back of the hospital. This building built in the early 1960s was the original nurse's home for Middlemore hospital. CMDHB has used this building for office accommodation since the closing of the nurse's home in the early 1980s. The concrete construction, small room size, low ceiling height and poor climate control place restrictions on the use of this building as a full treatment centre. Therefore the housing of CCRep may, not be displacing other clinical activities.

As identified in chapter 3, the Canadian Academy of Health Sciences (Panel on Return on investment in Health Research 2009b) identifies five impacts of applied clinical research: (1) advancing knowledge, (2) informing decision-making, (3) economic benefits, (4) capacity

building and (5) health benefits. Evidence from the current study to some extent supports this model. However, the results also suggests that psycho-social benefits such as the prestige gained by the hosting hospital, the motivation and satisfaction experienced by researchers and staff and the increased feeling of self-worth identified by participants are very important to the stakeholder groups. The study, therefore, suggest the addition of a psychosocial category to the Canadian Academy of Health Sciences model will provide additional recognition of these important benefits.

As reported in chapter 3, Watson identifies considerable benefits to the people of New Zealand in undertaking clinical trials. The results from the current study support all of Watson's suggested benefits except those relating to the sponsorship of education, health and community organisations. No informant identifies this as a benefit from clinical trials. This may be because pharmaceutical company sponsorship is not as common in New Zealand as Watson suggests or alternatively because pharmaceutical company sponsorship is not widely advertised and therefore our informants are not aware of it.

Getz (2008a) detects a North American feeling of public distrust in clinical research professionals and in the organisations responsible for research conduct within North America. Stakeholders do not distrust in the New Zealand environment. In contrast to the North American study, the current study suggests a general trust in clinical research professionals in New Zealand.

THE DISTRIBUTION OF BENEFITS AND COSTS

The distribution of benefits and costs is an important component of any BCA. While the general feeling is that both benefits and costs affect all stakeholder groups, the benefits out-weigh the costs, two groups of informants feel that their costs are greater than others. These members of the Maori political Party believe that their perspective is representative of Maori and researchers who had conducted non-sponsored research in the past. As the study did not separate informants by race, it is not known how many other informants were Maori or how representative the Maori Party view is. Their perspective is recorded separately below as it provides a different perspective from that of other informants.. Two groups were often singled out as receiving more benefits than others. These groups were the rich and pharmaceutical companies.

MAORI[5]

The Maori Party feels that Maori are disadvantaged by DHBs' focussing on sponsored clinical trials. The Maori Party supports a shift in the emphasis of health investment towards primary care whereby the Maori health workforce has equal work opportunities. They feel that clinical trials promote the over-use of pharmaceuticals in society. Pharmaceuticals are not a preferred treatment method by Maori – exemplified by many Maori who do not take prescribed medications. The Maori Party view clinical research as competing for health resources with the Maori health initiative Whanau Ora. Whanau Ora is a health promotion and disease prevention programme that is specifically for whanau (extended family). This involves promoting healthy lifestyles and practices to assist in minimising illness within whanau. Whanau Ora takes a holistic approach to well-being, which means taking into account the overall well-being of the whanau. They see Whanau Ora as the way forward to achieving a future where whanau determine what is in their best interests. It includes Maori concepts such as 1) Wairuatanga - spirituality, 2) Hinengaro - the mind, 3) Tinana - physical wellbeing, 4) Whanau - the family, 5) Whanaungatanga - extended family, 6) Waiora - total wellbeing for the family and individual, 7) Mauri - the life force, 8) Mana ake - the unique identity of the family and individual, 9) Ha a kui ma a koro ma - breath of life from our ancestors, 10) Whatumanawa - the open and healthy expression of emotion, 11) Whenua -reconnection to the land and 11) Whakapapa- maintain connections to whanau, hapu and iwi. The Maori party feels that DHBs can learn much from the old ways of Maori people.

An overemphasis on pharmaceutical treatments may undermine Rongoa Maori - the Maori traditional holistic system of healing and wellbeing programmes such as Tu Pou Tahi a health and wellbeing service set up for Rangatahi between the ages of 12 - 25 years throughout the Western Bay of Plenty and Tauranga regions promoting mental health, sexual health & suicide prevention. Clinical trials may compete for resources, with programmes such as Maori Mental Health Services for Tangata Whaiora (people seeking wellness). According to the Maori Party, there is evidence that Maori people do not get the same support as non-Maori particularly in the case of prescription medicines. Doctors may assume Maori people will not take their medicines

[5] Information for this section was gained by interviewing members of the New Zealand Maori Party.

and therefore, will not prescribe. This means pharmaceuticals tested on Maori may not be made available to Maori. Clinical trials are often located in the cities and Maori often live in rural centers so Maori may not get to participate in trials. The philosophy of Whanau Ora is that health systems should focus on the potential of people to navigate their own journeys. Government should give communities the ability to find their own solutions. They caution the danger that staff will be unduly influenced by pharmaceutical companies and develop an overemphasis on medications over other treatment sources. An overdependence on pharmaceuticals does not support Whanau Ora.

The Maori Party also believes that New Zealand needs to focus on strategies that bring about a change in attitude and behaviour and about leading healthy lives. By placing too much emphasis on pharmaceutical medications, a reliance on quick fix solutions may develop instead of tackling the route of the cause. They believe that money must be spent on facilitating Maori leadership in health services, ensuring the safety in health research and promoting effective support services. Rather than focusing on pill-popping cures for diseases New Zealand should focus on wellness checks like a warrant of fitness, these should be undertaken at least six-monthly minimum, but this should be dependent on the degree of risk. In addition, there should be regular checks for diabetes, asthma, cardiac and chronic disease that are prominent in Maori. This may prevent patients becoming reliant or dependent on medication for their treatment.

They observe that New Zealand has a small pool of specialists, and there is a danger of conflict of interests. They council that drug trials and pharmaceuticals are not benign and that we must be cautious in engaging in these trials. In addition, they warn that we need to be cautious about becoming dependent on research funds as a source of revenue for Health Boards and that there must be true separation of interests between boards and pharmaceutical companies. The Maori Party suggests that there must always be adequate central funding for health so that dependence does not arise. Finally, the Maori Party express the view that as Maori do not always have the same access to treatment as many non-Maori they are the most vulnerable in clinical trials, and therefore, carry the most risk of becoming teaching and research fodder.

One interviewee, a research nurse, who was confirmed that many Maori do not wish to take medications and therefore refuse to be involved in clinical trials. However, she feels that trials can be very valuable for Maori. Her findings show that some ethnicities tolerate some drugs better than other ethnicities. She finds one drug that is very effective and well tolerated by the

digestive system of Maori and Pacific Island people but given to Caucasian people, may produce severe diarrhea and they may be unable to continue its use.

RESEARCHERS NOT INVOLVED IN SPONSORED CLINICAL TRIALS

A small number of informants feel that researchers who are not involved in sponsored clinical trials do not receive the support and resources they need. This inhibits clinical areas from running their own research, and reduces the researcher's ability to use their expert judgment on what is worthwhile research. In addition, clinical areas that do not have the opportunity to engage in clinical trials may not have access to new treatments. Therefore, in order to undertake research in the hospital researchers must engage in clinical trials. Some suggest that researchers are often deployed into research that address insignificant questions such as the minor superiority of one drug over another, rather than more important questions of science. They feel that the health board undertakes sponsored trials en for financial reasons that may not be appropriate or are of minor importance to tDHB or patient group. One researcher suggests sponsored clinical trials take the place of research into questions worth asking and stifle free intellectual enquiry.

This is not, however, the view held by the majority of informants many of whom feel researchers engaged in sponsored clinical research develop valuable skills that builds confidence and encourages independent research. In addition, the sponsored trials earn revenue that can offset the costs of other internal non-sponsored research.

BENEFITS FOR THE RICH AND FOR PHARMACEUTICAL COMPANIES

A common concern among informants is that most people in the world do not get to benefit from clinical drug trials. They feel the pharmaceutical companies focus almost all of their effort on diseases that are prevalent in developed countries and almost none to the conditions that are prevalent in the developing countries. For example, there is very little pharmaceutical work going into malaria. In addition, even when there are investigations into drugs, which are prevalent in the developing world HIV, for example, the cost of those drugs are prohibitive. Clinical trials also create consumer led demand for some drugs over other health spending. It can twist the budget in favour of some sectors, for example, consumer led demand was created for Herceptin. One informant suggests drug trials are there to create demand for drugs from middle

class people. Some informants are concerned there is a risk of utilising poor communities for testing purposes.

One staff member suggests that the sponsor might seek to 'over' benefit financially from research by implementing findings to develop and manufacture drugs with a degree of exclusivity. If results are more openly available for use by all companies developing and manufacturing drugs, this could contribute to better global availability at an affordable cost minimising disadvantage to developing countries whose population health status may benefit from the use of the drug. In contrast to these views, one politician suggests that equity issues regarding access to medicines are a long running debate. He believes pharmaceutical companies have to develop the drugs before anyone can benefit but generic drugs are now produced in the poorer countries such as India and China, which benefit those countries sometimes at the expense of the large pharmaceutical companies that originally developed the drug.

One informant suggests clinical trials allow rich international companies to sell drugs and create dependencies. Some items like vaccines need a booster as they only survive in the body for a set period. There is an incentive for drug companies to push the use of their vaccine and then they lock the health system in to having to purchase the booster later. This takes money out of other areas of the health sector, and offshore. Related to this is the view that pharmaceutical companies are driving up the cost of health. Countries, who invest proportionately more of their GDP on health spend large amounts of money on drugs. The informant believes that DHB's should spend more money on primary health care and less on pharmaceuticals and believes we wait until people get sick and then give them expensive medications without any concentration on the cause of the illness. There is no evidence that pharmaceuticals are better than less expensive treatments. New expensive drugs are driving up the cost of health. New drugs are replacing older cheaper drugs with limited evidence of improvement. This benefits the pharmaceutical companies who are some of the wealthiest companies in the world.

KO AWATEA

In a move to provide balance to the range of research conducted at CMDHB and in response to some of the distribution issues identified above CMDHB has recently established Ko Awatea. Ko Awatea means first light – the first ray of sunshine that warms the day. Ko Awatea's goal is

to encourage people to think outside the square and come up with innovative ideas and initiatives. The goal is to take ideas that with the proper support, guidance and expertise can take the DHB from providing good care to one of providing outstanding care. It promotes the discovery of new knowledge and the capture and effective use of information. Ko Awatea focusses on specific needs of the organisation and coordinated knowledge to solve system challenges and issues. In addition, it provides a focus on both the quality improvement knowledge and technical skills needed to ensure healthcare is reliable in practice; and the knowledge and skills needed to appraise and evaluate scientific evidence and develop new healthcare interventions. Ko Awatea does not replace CCRep but works alongside it adding a new dimension to research at CMDHB.

CONCLUSION

This chapter describes the results of the multiple stakeholder perceptions strand. Sponsored clinical trials at CCRep involve a number of stakeholder groups: (1) trial participants (2) the family, community and other caregivers, (3) staff, (4) members of the pharmaceutical industry, (5) DHBs (6) the New Zealand community, and finally (7) the international community.

CMDHB and pharmaceutical industry representatives recognise that working together as research partners enhances their reputations and they express satisfaction from working in these partnerships and achieving the related synergies. Although a few respondents show concern about allowing the pharmaceutical industry to conduct trials in a public hospital, most feel that the trials benefit all groups involved. They express confidence in New Zealand's ethics process and in the research staff. Although some respondents, particularly hospital staff, express concern about the way in which trials are conducted overseas, the predominant belief is that trials in New Zealand are different. Respondents regard this as important because staff members' worries about ethical dilemmas and implementation issues are likely to cause reluctance to assist with trials in the future. Trust by the public in New Zealand based clinical trials is illustrated by the high recruitment success rates for clinical trials in New Zealand as reported by clinical research organizations and the pharmaceutical industry.

The results presented in this chapter indicate that the perceived benefits and costs cluster around a series of valued collaborative relationships in which each player gives something but gains

significantly in return. The collaborative relationships involve: (1) trial participants (2) the family, community and other caregivers, (3) staff, (4) members of the pharmaceutical industry, (5) DHBs (6) the New Zealand community, and finally (7) the international community. The pharmaceutical companies, DHB and researchers perceive that their reputations are enhanced by working together as research partners. There is general satisfaction among those involved in these collaborative relationships. In most cases, the benefits outweigh the costs and the group achieve synergies through working together. The relationship between the pharmaceutical companies and PHARMAC is the least harmonious. The pharmaceutical companies feel PHARMAC policies are too restrictive and present a barrier to the return that they can obtain in other OECD countries. PHARMAC regards the ever- increasing cost of new drugs as unsustainable.

In Chapter 5 reports the results of the economic outcomes strand of the study. This chapter, chapter 6 reports the results of the multiple stakeholders perceptions strand. The next and final chapter, chapter 7 concludes the thesis with a review of its principal findings, an overview of its contributions, and recommendations for future research.

7. CONCLUSION

This final chapter brings together the key research findings. It begins by restating the research question. A summary and discussion of the results of the empirical study follows. The chapter identifies the contributions and practical implications before detailing the strengths and limitations of the study and recommends areas for further research. The internal and external validity of the study are considered, followed by conclusions.

RESTATEMENT OF THE PROBLEM

As stated in chapter 1, the objective of this thesis is to address the research question: 'what is the value of conducting sponsored clinical trials in a publicly funded New Zealand hospital?'

REVIEW OF THE EMPERICAL STUDY

This thesis reports the results of an empirical study in which the value of conducting clinical trials in a publicly funded New Zealand hospital is analysed. The researcher considers the cost and benefits from several different perspectives.

The current study considers the benefits and costs from several different perspectives. The researcher first quantifies the benefits and costs from the perspectives of: (1) the Centre for Clinical Research and Effective Practice (CCRep); (2) Counties Manukau District Health Board (CMDHB) and (3) New Zealand society. It next establishes the benefits and costs of sponsored clinical trials as perceived by: (1) trial participants; (2) trial participants' family member and caregivers; (3) Counties Manukau District Health Board staff; (4) researchers; (5) the Counties Manukau community; (6) government, government bodies and politicians; and (7) members of the pharmaceutical industry.

The empirical study identifies the value of clinical trials by investigating economic data and stakeholder perceptions to produce a multi-level, multidimensional analysis of trial outcomes. As explained in chapter 4, the case study adopts a simultaneous parallel mixed method design combining qualitative and quantitative methods. This design builds on a health outcomes study conducted by a team of medical researchers that involves a retrospective cohort study of changes in participants' health status and mortality rates. The economic outcomes strand uses quantitative methods to estimate the benefits and costs of clinical trials. The multiple stakeholder

perceptions strand uses qualitative methods to explore the benefits and costs perceived by stakeholders.

This thesis presents the analysis of the economic outcomes strand from three perspectives by adapting a spreadsheet-based multiple account approach (Campbell and Brown 2003). The three sections of the spreadsheet reflect BCAs from three different but related perspectives, namely: (1) the CCRep research unit (micro-level), (2) the CMDHB (meso-level) and (3) New Zealand society (macro-level). The CCRep perspective draws data from profit and loss statements relating to the two trials.

The CMDHB perspective encapsulates the CCRep revenues and costs as well as CMDHB costs and savings from pharmaceutical and laboratory subsidies, patient treatment programmes, capital costs and infrastructure costs. The societal perspective builds on the CMDHB perspective and takes into account the changes in health status and value of lives saved as a result of the clinical trials. The researcher uses data reported in the health outcomes strand to calculate quality adjusted life years (QALY) and provide a measure of the societal benefits from clinical trials.

The multiple stakeholder perceptions strand reflects the perspectives of a range of stakeholder groups. The stakeholders are (1) trial participants (2) the family, community and other caregivers, (3) staff, (4) members of the pharmaceutical industry, (5) DHBs (6) the New Zealand community, and finally (7) the international community. The researcher uses several data collection processes including focus groups, surveys and interviews and it asks the same open questions of these stakeholder groups regardless of the data gathering process used. The researcher utilises the strengths of qualitative research, which enable the researcher to examine an issue, identify new ideas, and capture the outcomes that stakeholder groups perceive as relevant and important. This strand uses a qualitative descriptive analysis, coupled with a phenomenographical analysis, which allows the display of the data using the informants own words and then transforms the individual perceptions to conceptions that apply to a larger group.

SUMMARY AND DISCUSSION: RESULTS FROM ECONOMIC OUTCOMES STRAND

As reported in chapter 5, the empirical study includes a BCA from the perspectives of CCRep, CMDHB and society. The results present the economic benefits and costs of two trials conducted

over a period of eight years. From the perspective of CCRep, the surplus after considering costs and revenues is highest in 2002, after recruitment has begun. This is consistent across both trials and with the findings by Collier (2009a), Getz (2008a) and Kaitin (2006) discussed in chapter 3. The costs reduce during the trial period. The costs show a second peak at the end of the trial leading into the follow-up period. It is important that payments from sponsors be negotiated to meet these costs. Getz (2007a) finds that maintaining positive cash flow and profitability is a critical aspect of the operations management of clinical trials. The current study supports this finding. Schmitt, (2006) finds that research co-coordinators must negotiate trial budgets and contracts that are not too demanding or risky for their site. The current study assists this risk evaluation by highlighting the specific risk periods at the beginning and end of the trial.

The combined costs show a second peak at the end of the trial leading into the follow-up period. Troughs occur during the trial period in 2003 and at the start of the follow-up period in 2007. These peaks and troughs indicate that careful management is critical to ensure cash is available as needed. The results, therefore, support the view of Getz (2007a), that maintaining positive surplus and profitability are a critical aspect of the operations management of clinical trials and Schmitt, (2006) that co-coordinators must negotiate appropriate trial budgets and contracts that are not too demanding or risky for their site.

The researcher next considers the economic benefits and costs from the perspective of CMDHB. The researcher uses MOH and CMDHB data to identify the amount of cost avoided from pharmaceuticals, laboratory testing and CCM outpatient care because of participants being enrolled on the trial. The researcher finds that savings from cost avoidance from pharmaceuticals, laboratory testing and CCM outpatient care occur from the initial recruitment period until near the end of the trial period. This trend reverses at the end of the trial and into the follow-up period when the case group incurs higher costs. This finding suggests that the methodology used by Fireman et al. (2000) which restricts benefit cost studies to a one year time period early in the trial may limit the identification of potentially higher follow-up costs.

The results showing that savings from pharmaceutical cost avoidance is achieved only in three years over the study period is important. The current study finds pharmaceutical costs increase in the post-trial period. Perrín and López (2008) likewise identify cost increases for pharmaceuticals in the period immediately post-trial. Health Boards should consider the increase in post-trial pharmaceutical costs when negotiating contracts for clinical trials. Watson (2006)

suggests that public hospitals can realise significant cost avoidance because the trial sponsor pays the cost of trial pharmaceuticals. The researcher reveals that cost avoidance from pharmaceuticals occurs in only two of the eight years investigated. The CCRep clinical director (Personal communication 3/8/2010) suggests some reasons for the unexpected failure to obtain savings from cost avoidance of pharmaceuticals. The sponsoring companies cover most of the cost of pharmaceuticals during the trial period, which accounts for the cost saving on drugs in 2003-2006. The pharmaceuticals provided during the study were not funded under the New Zealand pharmaceutical schedule. As no subsidy was available on the study drugs, they were not made available in New Zealand. The pharmaceutical company withdrew the clinical trial drugs on completion of the study and participants were re-stabilised on different drugs (that is drugs that are approved for funding in New Zealand). The adverse event rate (i.e. the number of adverse events occurring within the case group as compared to the control group) may also have increased post-completion of the clinical trials as a result of this medication change. For example, participants got sicker than control group patients get and needed treatment that is more intensive. The clinical director also suggests that (personal communication 3/8/2010)

> *In addition, post-completion of the clinical trial, there would have been a period of intensive management and experimentation trying different drugs and dose-titration to customise the therapy. It is possible that this treatment review and dose-titration could have accounted for the increased cost of therapy (compared to the control group) in 2007-2009*.

A comment by a PHARMAC manager supports the above explanation; he suggests that there is considerable wastage of pharmaceutical products in physicians' attempts to find the right medication. While most studies in the literature focus on cost avoidance from pharmaceuticals they seldom mention cost avoidance from laboratory testing (see, for example, McDonagh et al. 2000, LaFleur et al. 2004). In the current study, the overall cost avoidance from laboratory testing is greater than that from pharmaceuticals. However, the savings from laboratory testing change as the trial progresses. The results indicate that CMDHB makes savings from laboratory test cost avoidance up until 2005. The cost of laboratory testing for the case group then increases above that of the control group in the period towards the end of the trial. One possible explanation for this increased expenditure on laboratory testing at the end of the trial is given by the clinical director of CCRep (personal communication 3/8/2010):

> *In the latter stages of one of the clinical trials (i.e. 2005-2006), there was an intensive drive from the clinical trial management group to meet the glycaemic target for the study (HbA1c <6.5percent) in all participants. This would have required more laboratory testing and may have accounted for the anomalous differential laboratory cost in 2005-2006*

An unexpected finding from the laboratory testing costs is the large drop in average costs per person following the change in contractors for laboratory services in 2007 – from $230 to $9 for the control group and $228 to $10 for the case group. This change was controversial and resulted in considerable resistance from the public and laboratory workers at the time. The only accessible measure of cost avoidance resulting from outpatient care is CCM. The researcher finds that fewer case group members than the control group members are enrolled in CCM. One possible explanation for this is that either members of the case group or their general practitioners feel that enrolment in a clinical trial provides sufficient support, or there is no need for additional treatment options. Another possibility is that the time involved in trial participants' attending both CCM appointments and trial appointments make it impractical to be enrolled in both.

In the final analysis, an economic assessment of the benefits and costs from the perspective of New Zealand society finds decreased mortality rates associated with the case group when compared to controls result in a benefit to New Zealand society of between $592,630 and $17,384,641 depending on the method used to calculate QALY. The researcher considers the distributive impact of the identified costs and benefits. An important finding of the multiple stakeholder perceptions strand is that the relationship between the pharmaceutical companies and PHARMAC is less harmonious than those among other groups. The pharmaceutical companies who rely on the sale of medicines at the end of the clinical trial to recover the cost of the trial feel that PHARMAC policies are too restrictive and preclude the return that they can obtain in other OECD countries, while PHARMAC regards the ever-increasing cost of new medicines is unsustainable. One possible explanation of the pharmaceutical companies' involvement in clinical trials in New Zealand may lie in the theory of legitimacy discussed in chapter 2. Sponsoring clinical trials may help build trust and, therefore, legitimise their organisations.

The economic outcomes strand supports the findings of the multiple stakeholder perceptions strand. Economic benefits from sponsored clinical trials for CCRep, CMDHB and New Zealand

society includes sponsorship from the pharmaceutical industry, which anticipates profits from the sale of medicines if the trials are successful. The researcher identifies wide differences in the value of QALY dependent on the method used. The pharmaceutical industry places a higher value on QALY than those generally used by decision makers in new health technology assessment (McGregor 2006). The wide difference in value between the investment per QALY made by PHARMAC and the assessment value of a QALY made by decision-makers may be a key to understanding the dissatisfaction of the pharmaceutical industry with PHARMAC. Each group places a different value on the benefits of the new drug and, therefore, the amount they feel is an acceptable price for the new drug. As discussed in previous chapters, while life has value (Chaiken 2003), placing a monetary value on life has been controversial (Samuel, Dirsmith and McElroy 2005). The researcher acknowledges that social valuations of QALY are ultimately ethical judgments (Abelson 2007) and New Zealand society may place a higher or lower value on saving lives than the values used in this study. For this reason two estimates of QALY are given in the current study. The current study only uses QALY to calculate the benefits and costs from the perspective of New Zealand society. QALY are most useful when making decisions at a societal level (Neumann 2011). Measuring QALY can never be exact and therefore cannot be relied upon in isolation as Neumann (2011 p 1806) highlight:

> *The QALY provides a convenient yardstick for measuring and comparing health effects of varied interventions across diverse diseases and conditions. It helps foster consistency and transparency in health care decision making. Rather than being a rule, it is intended to serve as a rough benchmark for health gains and as one of several inputs into decisions.*

SUMMARY AND DISCUSSION: RESULTS FROM MULTIPLE STAKEHOLDER PERCEPTIONS STRAND

This is the first study, to the researcher's knowledge, to compare the perceptions of clinical trials from seven stakeholder groups. Chapter 6 first applies a qualitative descriptive approach to analyse the results. The qualitative descriptive approach allows the stakeholders to express their perceptions and stories in their own words (Sandelowski 2000). In reporting the qualitative descriptive results, Chapter 6 stays close to the transcribed data in reporting the findings and frequently quotes the informants' views and experiences so that the accounts are theirs rather

than the researchers. Chapter 6 then presents the pheomenographical analysis. Phenomenography provides a systematic way to separate and describe different ways of experiencing phenomena. The following section brings together the key findings from each of the informant stakeholder groups and provides links to the contributions of some past studies discussed in chapter 3.

TRIAL PARTICIPANTS

Most of the informants from this stakeholder group feel that they benefit more from the clinical trial care than they do from the new medicine. They report that the trial provides them with benefits such as regular full check-ups, perceived better care, opportunities to learn about their illness and additional support from research staff. Some participants indicate that they value the satisfaction they gain from doing something to help others and from participating in an activity they describe as worthwhile and important.

Many informants identify their motives for enrolling in a trial. Their answers largely support the Mueller (2004) concept of contingency discussed in chapter 2. Mueller identifies contingency as a method for participants to identify and interpret uncertainty and also to control or manage that uncertainty. Mueller suggests that participants consider three kinds of contingencies before enrolling in a clinical trial (1) clinical (2) social and (3) technical.

Clinical contingencies assist potential participants to deal with failing health and limited care options. One informant engages a clinical contingency when they enrol in a trial as a means of obtaining additional follow-up treatment after their by-pass surgery. Social contingencies take three forms, altruism, trust and structure. The researcher finds many examples of participants enrolling in a trial for altruistic reasons. Trust in the advice given by the referring physician may influence the potential participant to follow the 'expert' advice and enrol. Structure provides an event or purpose to the often-unfocussed lifestyle of people with disabilities. One informant, an elderly woman is motivated to participate in the trial by the structure it provided to her week. She lives alone, and explains that prior to enrolling in the trial she was so lonely she would spend her days at the shopping mall. The trial gave her somewhere different to go and someone to talk to. When the trial ended, she returned to her seat at the mall. Participants use technical contingencies when they enrol in a trial to obtain technical information about their disability. Many of the informants have recently been diagnosed with diabetes. They view the trial as an opportunity to learn how they can best manage their illness.

FAMILY AND CAREGIVERS.

The researcher finds that family members and caregivers are generally happy for the trial participant to enrol in a clinical trial. They place a high value on the support and advice they gain from the research team. Many say this helps alleviate the isolation associated with being a sole care-caregiver. They suggest that although they invest their time in accompanying participants to their frequent trial appointments this is negligible compared to the gains from the support and education they receive. Family and caregivers appear reluctant to mention in the presence of the trial participants any inconvenience that they experience. However, when alone one, caregiver admits to finding it difficult to fit clinical trial activities around other responsibilities. In most instances, the caregiver's perceptions of clinical trials mirror those of the trial participants. The results support those of White (2004) who finds equally strong support for trials from both patients and their relatives.

Family caregivers play a central role in providing support for trial participants. Understanding the factors that influence the caregivers' abilities to cope in their supporting function is important as it allows research nurses to help ameliorate the burdens associated with this role and anticipate any problems that may arise.

CMDHB STAFF

Of all the stakeholder groups in this study, CMDHB staff identify the widest range of advantages and disadvantages resulting from clinical trials. Many reason that being involved in a clinical trial provides useful training and therefore expands their career opportunities. According to some staff, being on the trial team allows them to spend more time with individual trial participants. Involvement in trials has allowed many staff to build collaborative networks both internationally and domestically. Others suggest that trial involvement provides access to the latest developments in their treatment area and gives evidence on which to base future treatment choices, along with opportunities to travel and to publish results. Some feel that they gain prestige amongst their peers and become part of a pool of excellence that can be used to help others. Some staff members reveal that they have also been participants on clinical trials about which they have learned at their workplace. Overall staff members report an increase in satisfaction and motivation and believe their actions are making a difference to the future outcomes of their patients. They consider that having clinical trials in a hospital gives that

hospital more prestige and helps with the recruitment and retention of staff. While acknowledging the potential financial benefits of sponsored clinical trials to CMDHB, some staff members identify the potential risks of cost over-runs, under reimbursement, and dependence on the income from sponsors. They also have concerns about the opportunity costs associated with both staff and facilities. New Zealand has a robust system of ethical review that still has public support and confidence, Management and the multidisciplinary team generally identify a need for high ethical standards and quality consciousness in the conduct of clinical trials. As with other stakeholder groups the majority of management and staff are aware that if something does go wrong it is likely to lead to a loss of public trust.

RESEARCHERS

While most researchers view their jobs as both satisfying and rewarding, some feel that this comes at the cost of the loss of their flexibility and independence. Research nurses report that they gain satisfaction from working closely with participants over a long period. While most consider they are doing something worthwhile, others worry that the integrity of their research is undermined when it is viewed as a revenue gathering exercise, or a marketing activity. The perceptions of researchers and DHB staff regarding the personal benefits from involvement in clinical trials overlap considerably. Like DHB staff, researchers identify the benefits of high satisfaction, prestige, feelings of being at the frontier of medicine, the development of rewarding collaborative networks and the ability to publish their results. Researchers also value travel opportunities and increased career prospects. Many pride themselves on the high ethical standards and reliable drug testing in New Zealand. Some researchers, however, acknowledge the personal costs of their involvement in clinical trials including heavy workloads, being on-call 24 hours a day in case of adverse events and trying to fit the trial commitments around their normal clinical duties. The current study finds no evidence to suggest that research staff at CMDHB or CCRep feel undervalued. The study finds research nurses at CCRep feel they can have input into all aspects of the clinical trial process. They appear to be a well-recognised and valued part of the research team.

THE COUNTIES MANUKAU COMMUNITY

Many members of the Counties Manukau community are unaware that Middlemore hospital conducts clinical trials. The informants from the Counties Manukau community fall into two

distinct groups (1) those that have no experience and minimal knowledge of clinical trials and (2) those that have had active involvement with trials as a participant, a caregiver or a staff member. The study includes the first group above because they may be affected by clinical trials in the future. In addition as a tax payer they 'own' the facilities in which the clinical trials are conducted. The initial reaction of most of the informants who have no previous experience of clinical trials is to liken participation in a trial to being a '*guinea pig*'. They commonly refer to adverse reactions that the media report. The United Kingdom phase I trial, which resulted in six healthy volunteers becoming severely ill, has a negative impact on many of the community informants making them wary of clinical trials. Although apprehensive about participating in a trial, most concede that if faced with a potentially fatal illness a clinical trial may give them hope and motivate their involvement. In general this group sees advantages in having trials which ensure safe medicines and give participants a choice but have reservations about the consequences should something go wrong. Those who have had exposure to clinical trials are more positive about the benefits which they identify as an increase in the prestige of the hospital, economic benefits to the DHB and an increase in the quality of life for participants and their families.

GOVERNMENT, GOVERNMENT BODIES AND POLITICIANS

Most informants from this stakeholder group are aware of the wider benefits to the New Zealand community in hosting clinical trials and identify advantages such as gaining overseas currency, profiling New Zealand as a research centre, lifting national health standards and reducing the health care costs to the taxpayer. Some judge the resulting data from clinical trials as helpful for making decisions on health resource allocation. Informants view DHBs as benefiting from the prestige associated with conducting clinical trials. The trial also produces savings to the DHB, which owns the facilities because the trial covers the costs for the treatment of its patients who enrol in the trial according to one DHB member. Some politicians see trials as a way of broadening treatment choices and adding *'another dimension to the services that a DHB offers'* (politician). They view trials as beneficial to clinicians, medical researchers, and patients and see opportunities to undertake research into conditions of local importance. Many identify potential disadvantages, for example, the opportunity cost of having staff and facilities employed in clinical trials and the development of an overdependence on medicines at the expense of other treatment choices. Others worry about exposing New Zealand citizens to medical risk. They

often emphasise the importance of maintaining high ethical standards. One political party was very strong in its view that clinical trials reinforce a pharmaceutical model of treatment and in doing so marginalise other models of health. They fear that pharmaceutical products will potentially consume greater resources for fewer real health outcomes and because most pharmaceutical companies are internationally owned, they will drain their revenue from the New Zealand economy.

While some politicians support a liberal approach to clinical trials – that is, enrolling in a trial should be a matter of individual choice with minimal government interference – others adopt an equalitarian approach and therefore have concerns about the private sector being involved in the public health system. Most informants from this group have views between these two positions.

Two key reports were examined in chapter 2 (1) The House of Commons Health Committee (2005) and (2) the Watson Report (2006). The House of Commons Health Committee (2005), reports that in Britain the pharmaceutical industry has influence over all aspects of health and pharmaceutical care. The results show no evidence that the influence of the pharmaceutical industry in New Zealand has reached the level in Britain, although there are some fears that this may eventuate. The researcher suggests two possible reasons for the pharmaceutical industry's limited influence in New Zealand. First unlike Britain, New Zealand does not have a large domestic pharmaceutical industry and therefore the industry cannot exert the same economic pressure that it can in Britain. The pharmaceutical industry in the UK employs around 72,000 people directly (The Association of the British Pharmaceutical Industry 2011) and therefore can exert considerable influence. Second in New Zealand PHARMAC plays an important role in reducing the possible influence of the pharmaceutical industry on our health system.

PHARMACEUTICAL INDUSTRY

While most pharmaceutical representatives are happy to discuss health advantages to participants, they are quick to point out that there is a risk with any medical intervention including new drugs. They suggest that participants get high quality treatment on a trial because of the regular monitoring as well as potential health advantages from the new medical breakthrough. Many regard the moderate costs of conducting trials in New Zealand as an advantage but feel that delays experienced in obtaining ethical approval adds cost. Although some industry managers praise the quality of New Zealand research staff, others report difficulty in finding sufficiently qualified researchers to run their trials. One sponsoring company brings in

additional staff from overseas to work alongside local researchers because of skilled staff shortages. Others show concern over the lack of co-operation between research centres in New Zealand, which makes it difficult to run multicenter trials. They see opportunities for research centres to form strong linkages to establish a coordinated approach to promote their expertise to the pharmaceutical industry. Infrastructure is also important to one informant who indicates there is often insufficient clinical trial infrastructure investment by DHBs to ensure the viability of on-going contracts. He proposes DHBs ensure '*at least some of the income from clinical trials is used to improve the clinical trials infrastructure'* (representative).

There is also concern within the pharmaceutical industry that owing to PHARMAC's restrictive process for drug registration in New Zealand the pharmaceutical industry cannot guarantee continued access to medications for participants after completion of the trial. The industry informants suggest that it is not practical to introduce products that are not subsidised by PHARMAC, as the demand is small, the shelf life is often short and the importing costs high. The pharmaceutical industry sees the commercialising of new products and bringing them to market in New Zealand as high risk. They are critical of the time consuming and restrictive PHARMAC reimbursement process. Many in the industry feel that if PHARMAC lifts its restrictions, the number of trials in New Zealand would increase significantly. Lockhart, Babar and Garg (2010) support this view and identify '*a direct relationship between a country's pharmaceutical pricing and reimbursement policies and the pharmaceutical industry research and development investment in that country'* (p4).

The preceding section identifies a wide range of benefits for the international community, New Zealanders, the DHBs and their staff, participants and their support people. Clinical trials are vital to the improvement of medical care. The current study identifies benefits for the health system, benefits for education and benefits to the economy

The study has shown that there was a high degree of agreement overall amongst stakeholders concerning the overall value of clinical trials. There are however many differences between stakeholder groups in their perceptions of the costs and benefits. The differentiation between the stakeholder groups provides a basis upon which diversity in perceptions can be understood. The dimensions of value revealed in the study provide a basis for those involved in conducting clinical trials to proactively manage the formulation of strategy, performance management processes, and communication with stakeholders.

DIFFERENCES IN PERCEPTIONS

The results presented in this chapter provide a picture of the differences in the perceptions and values between stakeholders, which lead to differences in how they define the costs and benefits and therefore the value of clinical trials. Value, therefore, can take on different meanings depending on the perspective. This can bring competing perceptions of value across stakeholder groups. Quintiles (2011 p4) suggests these differing perceptions can be challenging

> *With physicians demanding further evidence of a new product's effectiveness, patients demanding more assurance regarding a drug's safety, payers demanding demonstrable proof of a therapy's value, and policy-makers demanding confirmation of a product's real-world risk/benefit profile in large populations, understanding what information to communicate to each group is a significant challenge for drug developers.*

Two theories help to explain why these differences may occur (1) means-end chain theory (Gutman 1982; Howard 1977; Young and Feigin 1975) and (2) differentiated reality theory Llewellyn (2007).

Means-end chain theory (Gutman 1982; Howard 1977; Young and Feigin 1975), discussed in chapter two provides an explanation as to why different stakeholder groups may perceive benefits and costs differently. The means-end chain theory assumes that stakeholder subjective perceptions of a service is the result of associations between its benefits and its costs (the 'means') and more abstract cognitive schemata, which include the personal values underlying certain behaviour (the 'ends'). These associations determine the value they place on the benefits and costs of the service in question (López-Mosquera and Sánchez 2011 and Reynolds and Gutman 1988). Applying this theory, the value of clinical trials from the perspective of each stakeholder is the degree to which the trial contributes towards the attainment of their desired end-state or goal. As stakeholders have different desired end-states they will perceive different benefits and costs, and value clinical trials differently. An example of this is the way participants view their transport to and from the clinical trial. While some stakeholders view this as a cost to participants, the participants themselves do not. This is because the participants view their transport to the trial as a means of obtaining the valued end-state of good health.

What a person judges as value depends on their focus – what Llewellyn (2007) calls differentiated reality. Value crosses the boundaries between the physical, structural, agential

cultural and physical realms. As discussed in chapter 1, Llewellyn (2007) distinguishes five differentiated realities that can provide an explanation for the wide range of costs and benefits identified in the study. The physical realm enables the identification of health outcomes in the study. Health outcomes include both the positive health improvements and the adverse drug reactions. The structural realm assists the identification of the structure policies and procedures that govern PHARMAC, the ethics committees, the treatment protocol and the operation of clinical trials. Some may perceive these structures as creating value and others as restricting the creation of value. The agential realm facilitates the feelings experienced from doing something worthwhile and doing something for future generations. The cultural realm enables the valuing of participant and caregiver education and the knowledge created by the trial that is transferred to standard clinical practice. Finally, the mental realm facilitates perception, thought, feelings, desires, emotions and predispositions.

THE DISTRIBUTION OF BENEFITS AND COSTS

A detailed analysis of the distribution of benefits and costs is beyond the scope of this thesis. The two strands of the current study do however allow for some general observations. The economic outcomes strand shows the distribution of costs across the micro (CCRep), meso (CMDHB) and macro (societal) layers of analysis. As discussed in chapter 5 the greatest economic benefit occurs at the societal level. The multiple stakeholder perceptions strand also identifies differences in the distribution of benefits and costs. As reported in chapter 6 two groups 1) Maori and 2) researchers involved in non-sponsored research feel disadvantaged by the clinical trial process. There are also two groups who respondents feel benefit most from clinical trials. 1) the rich and 2) the pharmaceutical companies. The general feeling is however that all stakeholder groups have both benefits and costs those benefits out-weigh the costs,

CONTRIBUTIONS

This study makes four important contributions; by 1) extending the application of BCA in the accounting literature, 2) enhancing value measurement in the health sector, 3) extending the application of mixed method research in accounting and 4) further developing method in the formation of a social report.

THE APPLICATION OF BCA IN ACCOUNTING

This is the first study, to the researcher's knowledge, to apply a spreadsheet-based multiple account approach (Campbell and Brown, 2003) to accounting within the health sector. As reported in chapter 5, the three sections of the spreadsheet for the economic outcomes strand of the study reflect BCAs from different but related perspectives, namely: (1) the CCRep research unit (micro level), (2) the CMDHB (meso-level) and (3) New Zealand society (macro-level).

The purpose of the BCA is to provide the decision maker with objective economic information to evaluate a programme (Campbell and Brown 2003). Separating the analysis into micro, meso and macro levels enables decision makers to consider the weight or importance they wish to place on each level. Different types of decisions will require different levels of analysis, for example, a decision on whether CCRep should conduct a trial may place maximum weight on the micro–level analysis whereas whether to encourage clinical trials within the public health system may require placement of the most weight at the meso level. The consideration of the relationships between these levels is also important. Increasing health costs and patient demand creates a need for the micro, meso and macro levels of the health system to work together to ensure the maximum benefits are achieved for all investments. The New Zealand Parliament Health Select Committee (2011) uses all three levels of analysis as part of their enquiry.

Accounting researchers in the health sector borrow extensively from economic literature. In the researchers view, benefit-cost analysis is important to accounting for the following reasons: First, benefit cost analysis uses accounting information such as costs and charges (Oakes, Considine and Gould 1994). Second, governments as funders of health-care look towards accounting to fulfill the three functions of measuring financial performance, allocating resources and controlling expenditure. Accurate benefit cost analysis assists these functions (Robson 2007, Chua and Preston 1994). Third, naturalistic (*in situ)* research investigating how accounting numbers are used in real situations can raise important disciplinary insights (Broadbent and Guthrie 2008, Baxter and Chua 2003, Oakes, Considine and Gould, 1994). In addition, an analysis of benefits and costs can provide the data needed for evidence-based financial management and provide critical data to support management decisions in health care (Finkler, Henley and Ward, 2003). Finally, it provides a framework for assessing the degree to which a project serves the 'public interest'. Accounting has a claim that it serves the public interest and

accounting scholars have been urged '*to promote not just accounting in the public interest, but accounting(s) that are in the public interest(s)'* (Neu and Graham 2005 p589). The International Federation of Accountants (IFA), (2010 p5) states that accounting bodies should:

> *....assess the public interest in terms of negative and positive outcomes (costs and benefits) for society as a whole, recognizing that the accountancy profession through its actions has an impact on people, organizations, capital markets, and governments.*

The IFA recommends that costs and benefits be assessed in both quantitative and qualitative terms. The current study shows that a blend of methods provides a rich and powerful means of evaluating the benefits and costs of clinical trials. The IFA distinguishes the application of BCA at a societal (macro) level from that at the project or investment (micro) level BCA appraisal undertaken by individual organisations seeking to maximize profit. The micro, meso and macro levels of the benefit cost analysis used in this study appear to meet this expectation.

THE MEASUREMENT OF VALUE IN HEALTHCARE

The current study expands the economic approach of BCA to incorporate non-economic benefits. The success of this integration suggests that an economic approach should be only one element to consider in measuring value in healthcare. As stated previously in this thesis, Porter (2008 p162) defines value as a '*measurement of patient health outcomes per dollar expended to achieve those outcomes'*. He specifies outcomes in the health system as total patient health outcomes rather than the services delivered at a clinical location, relates value to the customer rather than supplier and measures value by outcome, not inputs.

Outcomes can be difficult to isolate and define. The health outcomes of interest to the patient may not be the same as the outcome of interest to clinicians and researchers (Gray 2011). Although Porter (2008) defines value in terms of the relationship between costs and outcomes this is not a widely accepted view among all stakeholders. According to a study by Quintiles (2011 p 5):

> *Stakeholders have internalized the concept of value in very different ways, with biopharma executives as the only group in which a majority includes outcomes as part of their definition. For patients and physicians, the process (quality of care) appears to*

matter as much as the outcome when it comes to value, although nearly one-third of patients do not feel they can define value.

This lack of consensus on the meaning of value in healthcare influences the questions used in the multiple stakeholder perceptions strand of the current study. The researcher asks stakeholders about costs and benefits rather than to identify value created because these should be easier for stakeholders to identify and define.

Using Porter's model some health services (for example end of life care) are high cost while poor health outcomes are judged as low value. However, having the right kind of end of life care is of high value to patients and their families. From the patient's perspective Porter's focus on cost and outcomes is insufficient in this instance. As discussed in chapter 2, Gray (2011) takes a comprehensive approach when he identifies three key factors, (1) hotel amenities, (2) interpersonal and (3) technical /clinical, that influence patient experience. To understand how patients perceive value in healthcare requires a consideration of all three aspects of patient experience.

The current study incorporates process as a consideration when measuring value. The current study adopts the view that value is a measurement of treatment process experience combined with patient health outcomes per dollar expended to achieve those outcomes. The three strands of the current study design measure each of these value components. The economic strand measures costs. The multiple stakeholder perceptions strand measures process and the health outcomes strand measures health outcomes. Together they provide a comprehensive understanding of the value of clinical trials.

THE USE OF MIXED METHODS

Although researchers in the social sciences have used mixed methods research extensively since the 1980s this is not the case for the use of mixed methods in accounting. As Grafton, Lillis and Mahama (2011 p5) observe '*there is still little evidence or sustained discussion of mixed methods research in the accounting literature'*. Modell (2005) reviews the use of mixed methods in the accounting discipline and finds that the majority of mixed methods research involves a combination of surveys and interviews. A search by the researcher finds that accounting scholars most often use mixed methods for the triangulation or cross-validation of their research results

(see for example Davila and Foster 2007 and Graham, Harvey and Rajgopal, 2005). The current study extends the use of mixed methods in the accounting discipline in two ways. First it includes a mixture of methods not regularly used together in accounting research (surveys, interviews, focus groups and analysis of archived quantitative data). Second it applies complementary methods to assess two separate dimensions of one overarching research question. This motivation for using mixed methods research is not prominent in the accounting literature.

The researcher collects data on strands in parallel. The strands progress through parallel data collection and data analysis phases to produce independent outcomes. The rationale for using a combination of data sources is that mixed methods expose different views, perceptions and experiences of clinical trials. As Bryman et al. (2008, p. 264) suggest, if we view the evaluation of clinical trials as a large jigsaw puzzle, each method of data collection becomes '*an important piece of a jigsaw*'. Employing multiple collection methods for the multiple stakeholder perceptions strand, such as focus groups, observation and interviews can improve the validity, reliability and diverse identification of realities (Golafshani 2003). The researcher uses different methods for each stakeholder, for two reasons: (1) to recognise that relying on one method in isolation may give an incomplete view (Barbour 1998); and (2) to allow for communication preferences (Hoffman, 2009). The researcher asks the same questions of each stakeholder group irrespective of the data collection method used to facilitate a comparison of their responses. This uncovers differing perceptions; for example, health board staff members feel that trial participants gain the most benefit from the new treatment drugs being offered whereas trial participants identify the additional care and attention as the greatest benefit.

The study's findings are derived from the combined application of the complementary quantitative and qualitative methods that answer the different parts of the question. Hammond and Wiriyapinit (2005, p. 390) report the potential implications by comparing the findings from one method with those of another and identifying '*consistency (i.e. there was a match between findings), contrast (i.e. findings were contradictory)*' and '*complementarity [that] referred to findings derived from one method, which added a perspective unavailable, or simply not apparent, within the findings from a different method*'. They warn, therefore, that where there are many instances of complementarity, relying on one set of data alone risks giving a '*partial, even a misleading, impression'* of the phenomena under study (p. 391). In the current study the data are complementary in the sense that they produce a collage capable of delivering an

understanding of clinical trials in New Zealand; however, the data are not amenable to producing a meaningful composite. As data relating to many aspects of the study can be obtained via only one of the available research methods, the conclusion is that quantitative and qualitative methods can be combined in the current study only for complementary purposes.

Greene (2005, p. 209) observes that mixed method research '*offers greater possibilities than a single method approach for responding to decision-makers agenda, as well as to the interests of other legitimate stakeholders.*' Mixed method research realises these possibilities in the current study, given multiple and diverse stakeholders, including those who need hard data for their decision making and those who wish to understand the perceptions of the stakeholders.

ESTABLISHING THE FOUNDATIONS FOR A SOCIAL REPORT

This study incorporates multiple stakeholder perspectives and qualitative evaluation (Cotton, Fraser and Hill, 2000). It aids the development of social accounting and social audit in the public sector and addresses a need that has been identified in recent literature (Gray, Dillard and Spence, 2009, Ball, 2004, Marcuccio and Steccolini, 2005). The information elicited by this study provides evidence for the formation of a social report. While CCRep did not propose to provide such a report, it is now well placed to do so. Gray et al. (1997) identify three distinct types of statements that stakeholders make. These are

> (1) *things about which the accounting organization wishes to know; (2) information which each stakeholder would like to receive; and (3) their views (e.g. complaints) on the organization and its activities plus the activities and issues the stakeholders would like the organization to address* (p 349).

While the initial focus of the study was on CCRep, the relevance of other organisations, namely CMDHB and Central Government soon became apparent. This wider, tiered approach allows the researcher to identify examples of the above statement types. These organisations wanted to know about the experiences reported by the trial participants and staff. Participants said they wanted to receive information about the results of the trial from the researchers. The pharmaceutical companies wanted more transparency in the way PHARMAC makes resource allocation decisions. PHARMAC expressed a desire for more information about the impact of medications on Maori and Pacifica groups. Issues and activities that stakeholders would like

addressed include researchers wanting equity in the value placed on sponsored versus non-sponsored clinical research conducted in the hospital and pharmaceutical companies wanting greater access to the New Zealand market for their researched medicines.

Gray et al. et al. (1997) regard the development of the social report as the responsibility of the organisation concerned (1997, p339):

> *for predominantly practical (even pragmatic) reasons, we believe the systematic development of social accounting requires that the organization be the reporting body. As such, it is the business of the reporting organization to construct the social account; and such a social account, to be complete, must, we infer, recognize the voices of the stakeholders*.

The researcher asks stakeholders to consider the benefits and costs of clinical trials as they relate to themselves and other stakeholder groups. This raises awareness of both complementary and conflicting stakeholder interests. Although consensus among competing stakeholder interests is not the aim of this research, the process has the potential to bring about greater understanding between stakeholder groups. Hill et al. (2001 p6) observe that

> *The audit process may enhance communications and health care decision legitimacy, and improve both transparency and accountability to the stakeholders with whom the organisation is involved. These accountable stakeholder relationships are traditionally characterised by the quality of trust and by reciprocal responsibilities. Thus, the audit process may itself generate an increase in shared understanding and trust by building upon existing co-operative relationships.*

While the social audit serves as a '*voice*" for stakeholders, the process of social auditing can have additional positive outcomes. Ghonkrokta and Lather (2007 p 18) find that the social audit process

> *creates confidence in society regarding government initiatives, promotes transparency and efficiency, improves social, ethical and environmental performance, enhances inclusion, facilitates monitoring and ensures accountability.*

PRACTICAL IMPLICATIONS

The viability of conducting clinical trials in publicly funded hospitals in New Zealand depends fundamentally on the ability to create benefits for stakeholders. There is considerable value arising from clinical trials. By more clearly defining this value, New Zealand is better able to create a research environment that is capable of producing it. The New Zealand clinical research community is relatively small, generally supportive of each other and collegial. New Zealand has a generally creative and innovative culture. To gain the maximum benefit from hosting clinical trials, New Zealand must ensure that it is at the forefront of clinical trials in terms of scientific robustness, speed of start-up, ethical integrity and cost efficiency.

New Zealand must however balance the interests of the multiple stakeholders affected by clinical trials: those that may potentially gain present and future benefits and those that pay the cost. It is trial participants who bear the immediate impacts of any harms that may arise when participating in clinical trials. They do so willingly but are not always aware of the potential risk. New Zealand Health and Disability Ethics Committees are correctly placed within a sound legislative framework. Researchers and the pharmaceutical industry are rightly calling for the government to improve the speed of the trial application and approval process, especially the ethical review process Any actions to improve the efficiencies of review must not, however, undermine the ethical review process that protects the interests of trial participants and the community.

In addition, encouragement to increase sponsored clinical trials in New Zealand should not compromise the negotiating strengths and economic gains achieved by PHARMAC for the benefit of all New Zealanders. Those who are not immediately involved have little understanding of the extent and nature of clinical trials in New Zealand. There is a small stream of media reports highlighting ongoing research discoveries and developments within New Zealand however, increasing public knowledge and awareness of clinical trials, through regular media releases and providing information about ongoing research and development may assist understanding and aid participant recruitment.

There are a number of opportunity costs of using New Zealand's small research resource for conducting sponsored clinical trials, in particular qualified staff and research facilities. The current study identifies disadvantages to focusing only on sponsored clinical trials. Pharmaceutical companies may terminate trials if the 'market place' changes and show limited

interest in trials that might seek to determine the minimal duration of therapy, lowest effective dose and exploration of the role of older unpatented medicines. It may be useful for New Zealanders to consider opportunities for value creation and value capture along the whole pharmaceutical research pathway, not just at the clinical trial level. Getting to clinical trial stage for potential pharmaceuticals is only one stage on a continuum that begins with research based on cell physiology and biochemistry, bio-engineering, to potential product trials, and later product production and marketing.

Researchers located within DHBs conduct most sponsored clinical trials in New Zealand. With access to qualified staff, facilities and patients, DHBs provide a safe research environment. Occasionally respondents in this study describe clinical trials as a 'distraction' from clinical practice and an 'overhead', yet the study provides evidence that shows CMDHB benefits from this research. The study demonstrates that the CCRep business model of separating research and health provision roles within the DHB by establishing semi-autonomous clinical trial business units that are responsible for their own administration and infrastructure but are still able to access databases and specialist equipment on a fee for service basis when required is successful. New Zealand currently conducts mainly phase 3 and 4 trials. A move into phase I and II trials is may be possible given the size of many trial centres in New Zealand.

As discussed in chapter 1, there is currently no readily available information on the conduct of clinical trials in New Zealand. What gets measured gets focus, the value of clinical trials in New Zealand might improve by DHBs publishing quarterly data such as the number of trials conducted, turnaround time for trial applications, cost of trials, percentage of trials by phase, percentage of trials by therapeutic area and the sources of funding for trials (commercial or academic, local or international).

This study provides evidence to support the recently released recommendations of the New Zealand Parliament Health Select Committee to improve New Zealand's environment to support innovation through clinical trials (The New Zealand Parliament Health Select Committee 2011). The New Zealand clinical research industry is valuable. It produces both tangible economic benefits and less tangible but no less valuable benefits perceived by the stakeholders. It may now be appropriate to consider ways that industry, central government, DHBs and academic institutions can work together to promote New Zealand as a good place to conduct clinical trials. This challenge requires all involved with clinical trials in New Zealand to drive to continuously

improve upon the service they provide, the goal being to establish a competitive advantage through quality research outcomes and best practice activity. Protection of trial participants is paramount; rigorous independent ethics committee review, research approvals and monitoring of trials must continue.

Notwithstanding divergent perceptions of value and widely contrasting views of stakeholder groups, there seems to be support for the continuation of clinical trials in publicly funded hospitals in New Zealand. By engaging all stakeholders toward a common purpose of value creation, the health sector in New Zealand and elsewhere will be better able to withstand the many challenges ahead.

STRENGTHS OF THE STUDY

While acknowledging its limitations this study is significant as it represents a unique contribution to the existing knowledge on clinical trial policy and practice within New Zealand. It provides strong evidence of differing patterns of costs and benefits during the three stages of a clinical trial – pre-trial, trial and follow-up. The initial recruitment begins in June 2001 and the follow-up period ends in July 2009. The average per participant surplus after considering costs and revenue is highest immediately after recruitment has begun. This is consistent across both trials. In trial 1, a second peak occurs at the end of the trial and prior to the follow-up period. The trial period produces the lowest surplus for both trials under investigation. The cost revenue stream for trial 1 dips below zero during the trial period. It again dips below zero for both trials at the start of the follow-up period. These peaks and troughs indicate that careful management is critical to ensure cash is available as needed. Rather than focus on the full period of the clinical trial future studies should consider the benefits and costs that occur in each of these stages.

In addition, this is the first study of clinical trials in New Zealand, which brings together the views of key stakeholder groups and compares their perception of clinical trials. The approaches to stakeholders met with a strong response, indicating their willingness to be involved in the study and communicating their views. Informants tell their stories freely. When asked to consider issues from the perspective of other stakeholders many informants admit they have not considered clinical trials from that perspective before. Almost all informants want to see a copy

of the results. Executive members of the RMI travelled from Wellington to Auckland to discuss the results with the researchers.

The Report of the New Zealand Parliament Health Select Committee (The New Zealand Parliament Health Select Committee 2011) makes a series of recommendations to government to improve the competitiveness and attractiveness of New Zealand as a location to undertake clinical trials. It provides a comprehensive review and strategy for the future and lists a series of clear targets for government action, stating (p5):

> *Our key recommendations should be acted on urgently (within 12 months of this report's presentation) and aim to:*
>
> - *simplify and streamline ethical review processes*
> - *promote collaboration between Government departments to coordinate the system*
> - *develop a national health research action plan to foster innovation and commercialisation*
> - *develop a framework for clinical trial research throughout district health boards, to be facilitated by a hub.*

The report highlights the potential that exists in New Zealand to improve its capacity for clinical trials and acknowledges the key role that DHBs will play in achieving the proposed goals.

FURTHER RESEARCH.

This study provides measures of the benefits and costs of two clinical trials performed in a publicly funded New Zealand hospital. In doing so the researcher acknowledges the wisdom of Van Peursem, Pratt and Lawrence who suggest '*measures are an indication of a situation which may call for further enquiry. Indicators do not provide answers; they inspire questions*' (1995 p60). The current study suggests key areas for further research.

First, the methodology used provides a means of understanding stakeholder perspectives not found in published case studies or other research literature. Further research will help determine how effectively this research framework can be used to measure value in other areas of the health sector.

The current study has focused on two low risk, phase III clinical trials. Risk is an integral part of value for money analysis (Heald 2002). The trials in this study resulted in health benefits for the

participants. This may not apply in all studies. In particular, phase I and II trials may pose a greater risk. Further research may determine how widespread the findings are among other trials and trial participants.

The results showing that savings from pharmaceutical cost avoidance is achieved in only three years over the study period also requires further investigation. Additional research may assess if the patterns observed in the current studies are similar to other trials. Further investigation may also provide a better understanding of the cost drivers during the course of a clinical trial.

INTERNAL VALIDITY

Internal validity has to do with the accuracy of the results. Several factors relating to the selection of informants may have influenced the internal validity of the multiple stakeholder perception strand of this study. As involvement in the survey research is voluntary, informants are largely self-selecting and thus their views may not be representative of the population from which they are drawn. Staff and researchers have to complete the survey during the course of their busy work schedules. This research was unlikely to be their first priority and therefore not all those who have views on the topic may have completed the survey.

As focus groups include trial participants and caregivers, some caregivers may have been reluctant to admit costs to themselves in presence of trial participants. Informants taking part in the focus groups are required to find their own transport to the study location. A few who were too disabled to travel independently turned down the opportunity to participate. Although the researcher gives these potential participants the opportunity to complete a written survey, some are too unwell to cope with any research activity and decline to join the current study. It is possible that those who decline to complete the survey or participate in a focus group have lower levels of motivation and attitudes towards clinical trials. Consequently, this may have had the effect of higher positive attitudes towards clinical trials than might otherwise be the case. The researcher invites undergraduate students to represent the Counties Manukau community. Although these are part-time students and they include a wide range of age groups these informants in general have a higher educational background than the average Counties Manukau resident, which may have produced a more measured response. Informants return some surveys with incomplete or shortened answers when compared with in-depth interviews and focus

groups. Possible reasons for this are informant's time factors, not fully understanding the question or skipping questions if they feel they have nothing significant to report.

There are also threats to the internal validity of the economic strand of the current study. As discussed in chapter 4, the researcher uses the same platform of case and control groups as was selected for the health outcomes strand conducted by researchers at CCRep. While the CCRep research team went to some lengths to ensure that the groups were well matched, there is a possibility of selection bias (i.e. subjects are selected for clinical trials on the basis they are expected to survive till the end of the study). There is also the possibility that the 'control group' are not the same as the 'case group' (i.e. controls may have worse disease and a worse outcome and the outcome is really artefact) which may have influenced the study outcome.

While the study has been useful in indicating the possible scope of benefits and costs associated with sponsored clinical trials in a publicly funded New Zealand hospital, the findings relate to two trials in a specific hospital in a particular region. It is therefore necessary to exercise caution in applying these findings to other situations. The clinical data originates from the work of other researchers, which can be open to issues over control. The author believes however that there are adequate controls within CCRep to make this data reliable. The researcher sources much of the qualitative data used here from interviews and surveys. It is inevitable that such data will be subjective and, on occasion, may be designed to present the best impression, though they author does not believe this was generally the case.

While one study cannot answer all the questions a DHB might have about the benefits and costs of conducting sponsored clinical trials, this study should encourage DHB members to consider the impact of clinical trials in their district, lead to greater understanding of the dynamics of clinical trials and provide a common framework and rational for assessing the related benefits and costs.

EXTERNAL VALIDITY

External validity has to do with the generalisability of the findings to the population. The internal validity issues discussed in the previous section reduce the generalisability of the results of this study. In qualitative research, the research context limits the transferability of the results to other

contexts. The clinical trials involved in this study are located at CCRep, in Counties Manukau. This circumscribed location of the trials necessitates caution in making generalisations.

The researcher conducts this study at a single institution that conducts a high-volume of sponsored clinical trials within New Zealand. In addition, this study involves participants from two relatively low risk clinical trials. As such, their experiences may not be representative of all people who participate in trials and may thus limit the generalisability of the findings reported here. However, the variety of experiences described and the ease with which participants expressed their opinions (both positive and negative) allow the researcher to interpret the results with some confidence.

CONCLUSION

This is the first empirical study of the benefits and costs of sponsored clinical trials in a publicly funded New Zealand hospital. This study provides evidence that contributes to an understanding of the outcomes of clinical trials in New Zealand. In doing so, the study contributes to the existing knowledge of the value of clinical trials by illuminating the positions of varied stakeholder groups with interests in the policy, practice and outcomes of clinical trials. The application of qualitative and quantitative methods to analyse these interest-positions produces a more rounded analysis than would result from either approach on its own.

This thesis first quantifies the benefits and costs from a micro, meso and macro perspective and then establishes the benefits and costs of sponsored clinical trials as perceived by seven different stakeholder groups. The study contributes to the development of value theory by considering value at several levels and from multiple perspectives. It identifies the usefulness of BCA as a tool to assess value and demonstrates the importance of perspective in understanding the outcomes of a BCA. Although measuring qualitative characteristics is often a challenge, this study makes use of focus groups and interviews as a possible way to mitigate the limitations of BCA that use quantitative data alone. It establishes a basis for encouraging other people to use similar qualitative methods.

This thesis cannot determine the value of clinical trials because value is perceived by different people in different ways. However it does provide the means to consider the question of value more systematically and with greater depth than previous methods.

LIST OF REFERENCES

Abernethy, M. A., Chua, W. F, Luckett, P. F. and Selto, F. H. (1999), Research in managerial accounting: Learning from others' experiences. *Accounting and Finance,* Vol.39 No 1, pp.1-27

Abelson, P. (2007), *Establishing a monetary value for lives saved: Issues and controversies*, Working papers in cost benefit analysis WP 2008-2, Australian Government, Department of Finance and Deregulation, Accessed 18 November 2010 from http://www.finance.gov.au/obpr/docs/Working-paper-2-Peter-Abelson.pdf

Access Economics (2003), *Exceptional returns, the value of investing in health R&D in Australia*. The Australian Society for Medical Research.

Access Economics (2008a), *Exceptional returns: The value of investing in health R&D in Australia II.* The Australian Society for Medical Research.

Access Economics (2008b), Dementia Economic Impact Report. Alzheimers New Zealand Incorporated.

Accounting Standards Steering Committee (1975), *The Corporate Report*, Accounting Standards Steering Committee, London, UK.

Adler, M. D. and Posner, E. A. (2006), *New Foundations of Cost-Benefit Analysis*. Cambridge, MA: Harvard University Press.

Allen D. (1996), Costs, values and prices. *Management Accounting (UK)* Vol 74, No.4, p.32.

Anden, A., Andersson, S.O. and Rudebeck, C. E. (2005), Satisfaction is not all – patients' perceptions of outcome of general practice consultations, a qualitative study. *BMC Family Practice*, Vol. 6 No 43. Retrieved 19 September 2010 from http://www.ncbi.nlm.nih.gov/pubmed/16242048

Anderson, S. W. and Widener, S. K. (2007), Doing quantitative field research in management accounting, in Chapman, C. S., Hopwood A. G. and Shields, M. D. (Eds.), *Handbook of Management Accounting Research,* Vol. 1, pp. 319-41.

Angell, M. (2004), *The truth about the drug companies: How they deceive us and what to do about it.* New York: Random House.

Angell, M. (2008), Industry-sponsored clinical research: A broken system. *Journal of the*

American Medical Association Vol. 300; No. 9, pp.1069 -1071.

Auckland District Health Board (2006), Press release Retrieved 13 September 2010 from http://www.dontriskourhealth.com/ADHB_update_140706.html

Australian Government (2004), *Sustaining the virtuous cycle for a healthy, competitive Australia*. Canberra.

Australian Government (2007), *Best practice regulation handbook*. Canberra.

Australian Government (2008), *Best practice regulation guidance note value of statistical life.* Canberra.

Ayuso, S., Rodriguez, M. A. and Ricart, J. E. (2006), Responsible competitiveness at the ''micro'' level of the firm. Using stakeholder dialogue as a source for new ideas: a dynamic capability underlying sustainable innovation. *Corporate Governance,* Vol. 6 No. 4, pp. 475-490.

Babour, R. S. and Barbour, M. B. (2003), Evaluating and synthesizing qualitative research: the need to develop a distinctive approach. *Journal of Evaluation in Clinical Practice*, Vol **9** No.2, pp. 179–186.

Bagust A. and Beale, S. (2005), Modelling EuroQol health-related utility values for diabetic complications from CODE-2 data. *Health Economics* Vol. 14, pp.217–230.

Baker J. (2001), Nurses' perceptions of clinical decision-making in relation to patients in pain, a thesis submitted for the degree of Doctor of Philosophy, Department of Family and Community Nursing, Faculty of Nursing, The University of Sydney

Ball, A. (2004). A Sustainability Accounting Project for the UK Local Government Sector? Testing the Social Theory Mapping Process and Locating a Frame of Reference, *Critical Perspectives on Accounting*. Vol 15 No. 8, 1009 – 35.

Baltussen, R.M., Adam, T., Tan Torres, T., Hutubessy, R.C., Acharya, A. and Evans, D.B. (2002), Generalized Cost-Effectiveness Analysis: A Guide. *Geneva, World Health Organization, Global Programme on Evidence for Health Policy*.

Barbour, R. S. (1998), Mixing qualitative methods: Quality assurance or qualitative quagmire? *Qualitative Health Research,* Vol 8 No.3, pp. 352-361.

Barnard, A., McCosker, H. and Gerber, R. (1999), Phenomenography: a qualitative research approach for exploring understanding in health care. *Qualitative Health Research* Vol. 9 No. 2, pp. 212-226.

Barrett, J and Scott, C. (2008), Costs and funding of New Zealand local authorities: the role of democratic discourse. *International Journal of Public Sector Management* Vol. 21 No. 3, pp. 295-304

Bastian, H. (1998), Speaking up for ourselves: The evolution of consumer advocacy in health care. *International Journal of Technology Assessment in Health Care,* Vol 14 No.1, pp. 3-23

Baum, M. (1990). *The ethics of clinical research*. London, King's Fund.

Baum, S. D. (2010) Value typology in cost-benefit analysis. Environmental Values, forthcoming. Accessed 14/4/2012 from: http://sethbaum.com/ac/fc_Value-CBA.html

Baxter, J and Chua, W. F. (2003), Alternative management accounting research— whence and whither. *Accounting, Organizations and Society* Vol. 28, pp. 97–126.

Bazeley, P. (2007), *Qualitative data analysis with NVivo*. London: Sage

Beal, K., Dean, J., Chen, J., Dragaon, E., Saulino, A, and Collard, C. (2004), Budget negotiation for industry-sponsored clinical trials. *Anesthesia & Analgesia*. Vol 99 No.1, pp.73–76

Beauchamp, T.L and Childress, J.F. (1994)*, Principles of biomedical ethics*. New York: Oxford University Press.

Beauvais, B; Wells, R. (2006) Does money really matter? A review of the literature on the relationships between healthcare organization finances and quality. *Hospital Topics* Vol 84. No. 2, pp. 20-28.

Bechhofer, F. (1974), Current approaches to empirical research: some central ideas, in Rex, J. (Ed.), *Approaches to Sociology: An Introduction to Major Trends in British Sociology*, Sage, London.

Belal, A. R. (2002), Stakeholder accountability or stakeholder management? A review of UK firms social and ethical accounting, auditing and reporting (SEAAR) practices. *Corporate Social Responsibility and Environmental Management*, Vol 9, No. 1 pp. 8–25.

Bell, D., Bringman, J., Bush, A. and Phillips, O. (2006), Job satisfaction among obstetrician-gynecologists: A comparison between private practice physicians and academic physicians. *American Journal of Obstetrics and Gynecology,* Vol 195, pp. 1474–1478.

Bendheim, C. L., Waddock, S. A. and Graves. S. (1998), Determining best practice in corporate-

stakeholder relationships using data envelopment analysis. *Business* and *Society* Vol 37 No.3, pp.306-339.

Bennett, C., Adams, J., Knox, K., Kelahan, A., Silver, S. and Bailes, J. (2001), Clinical trials: Are they a good buy? *Journal of Clinical Oncology:* Vol 19 No.23, pp. 4330-4339.

Birmingham, B. A. (2006), *Value creation and value capture in non-profit partnerships*. A thesis submitted for the degree of Doctor of Philosophy, Antioch University Ohio USA.

Bititci, U. S., Martinez, V., Albores, P. and Parung, J. (2004), Creating and managing value in collaborative networks, *International Journal of Physical Distribution & Logistics Management*, Vol. 34 No. 3/4, pp. 251-268

Bloomfield, B. P., Coombs, R.W., Cooper, D.J. and Rea, D.M. (1992), Machines and manoeuvres: Responsibility accounting and the construction of hospital information systems, *Accounting, Management, and Information Technology*, Vol. 2 No. 4, pp. 197-219.

Blumenfeld, W, (1961) Value and valuation. *Philosophy and Phenomenological Research*, Vol. 21, No. 3, pp. 314-332 Published by: International Phenomenological Society Stable URL: http://www.jstor.org/stable/2105149.

Boardman, A. E., Mallery, W. L. and Vining, A. R. (1994), Learning from ex ante/ ex post cost benefit comparisons: The Coquihalla Highway example. *Socio-Economic Planning Sciences,* Vol 28 No 2, pp. 69-84.

Boardman, A., Greenberg, D., Vining, A. and Weimer, D. (2006), *Cost-Benefit Analysis: Concepts* and Practice (3rd ed). Prentice Hall: New Jersey.

Bok, S. (1978), *Lying*. New York: Pantheon.

Boselli, R., Cesarini, M. and Mezzanzanica, M. (2011), Public service intelligence: Evaluating how the public sector can exploit decision support systems, A paper presented at the European Association for Research on Services (RESER) conference 07 - 10 September Hamburg, Germany

Booth, R. (1997), Appreciating the Value before Counting the Cost. *Management Accounting* Vol 75, No. 1 pp. 54-56.

Boulding, K. E. (1956), Some contributions of economics to the general theory of value. *Philosophy of Science,* Vol 23, No.1, pp. 1-14.

Bourguignon, A. (2005), Management accounting and value creation: the profit and loss of reification. *Critical Perspectives on Accounting,* Vol 16 No. 4, pp. 353-389

Bowman, C. and Ambrosini, V. (2010), How value is created, captured and destroyed, *European Business Review*, Vol 22 No. 5, pp.479 - 495

Boyce, G. (2000), Public discourse and decision making: Exploring possibilities for financial, social and environmental accounting. *Accounting Auditing & Accountability Journal*, Vol. 13 No. 1, 2000, pp. 27-64.

Brannen, J. (2005), Mixing methods: The entry of qualitative and quantitative approaches into the research process. *International Journal of Social Research Methodology,* Vol 8 No.3, pp. 173-184.

Braunholtz, D., Edwards, S., and Lilford, R. (2001), Are randomized clinical trials good for us (in the short term): Evidence of a "trial effect". *Journal of Clinical Epidemiology*, Vol 54 No. 3, pp. 217-214.

Brewer, J. and Hunter, A. (1989), *Multimethod research: A synthesis of styles.* Newbury Park, CA: Sage.

Brewer, J. and Hunter, A. (2006), *Foundations of Multimethod research: Synthesizing styles.* Newbury Park, CA: Sage.

Broadbent, J. and Guthrie, J (2008), Public sector to public services: 20 years of "contextual" accounting research, *Accounting, Auditing & Accountability Journal* Vol. 21 No. 2, pp. 129-169.

Broadbent, J. and Laughlin, R. (1998), Resisting the new public management: absorption and absorbing groups in schools and GP practices in the UK, *Accounting, Auditing & Accountability Journal*, Vol. 11 No. 4, pp. 403-35.

Broadbent, J., Laughlin, R. and Read, S. (1991), Recent financial and administrative changes in the NHS: A critical theory analysis, *Critical Perspectives in Accounting,* Vol. 2 No. 1, pp. 1-29.

Bromwick, M., (1977), The use of present value valuation models in published accounts. *The Accounting Review*. July pp. 587-596.

Brouwer, W., Culyer, A., Van Exel, N., and Rutten, F. (2008), Welfarism vs. extra-welfarism. *Journal of Health Economics*, Vol 27 No 2, pp. 325-338.

Brown, M.L., Riley, G.F., Schussler, N. and Etzioni, R. (2002), Estimating health care costs

related to cancer treatment from SEER-Medicare data. *Med Care,* Vol 40 No. 8 suppl. IV pp.104-117.

Brown, T., Champ, P., Bishop, R. and McCollum, D. (1996), Which response format reveals the truth about donations to a public good?' *Land Economics,* Vol 72, pp. 152-66.

Bryer, R. A. (1994), Why Marx's labour theory is superior to the marginalist theory of value: The case from modern financial reporting. *Critical Perspectives on Accounting* Vol.5, pp. 313-340.

Bryer, R. A. (1999), Marx and accounting, *Critical Perspectives on Accounting*. Vol. 10, pp. 683-709.

Bryman, A. (2001), *Social research methods*. Oxford, UK: Oxford University Press.

Bryman, A. (2006), Paradigm Peace and the Implications for Quality *International. Journal. Social Research Methodology* Vol. 9, No. 2, pp. 111–126.

Bryman, A. (2007a), The research question in social research: What is its role? *International Journal of Social Research Methodology,* Vol.10 No 1, pp. 5 -20.

Bryman, A. (2007b), Barriers to integrating quantitative and qualitative research. *Journal of Mixed Methods Research* Vol 1, pp.8–22.

Bryman, A., Becker, S. and Sempik, J. (2008), Quality criteria for quantitative, qualitative and mixed methods research: A view from social policy. *International Journal of Social Research Methodology*, Vol. 11, No. 4, pp. 261–276

Burnet, K., Earl H., Charge H., Cox K., Benson J. and Purushotham, A.D. (2004), A survey of breast cancer patients' views on entry into several clinical studies. *European Journal of Cancer Care,* Vol 13, pp. 32–35.

Burrell, G and Morgan, G (1979), *Sociological Paradigms and Organisational Analysis*, Hants: Ashgate.

Bushfield, J. (2006), Pills, power and people: Sociological understandings of the pharmaceutical industry, *Sociology*, Vol 40, pp. 297–314.

Buxton, M., and Hanney, S. (1996), How can payback from health services research be assessed? *Journal of Health Services Research Policy*, Vol 1, pp. 35-43.

Buxton, M., Hanney, S. and Jones, T. (2004), Estimating the economic value to societies of the impact of health research: A critical review. *Bulletin of World Health Organization,* Vol 82 No. 10, pp.733 - 739.

Campbell, H. and Brown, R. (2003), *Benefit-cost analysis: Financial and Economic Appraisal using Spreadsheets*. Melbourne: Cambridge University Press.

Canadian Coordinating Office for Health Technology Assessment (1997), *Guidelines for Economic evaluation of pharmaceuticals: Canada*. 2nd ed. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA).

Carter, M. A. (2009), Trust, power and vulnerability: A discourse on helping in nursing. *Nursing Clinics of North America.* Vol 44 No.4, pp. 393-405.

Carter, R. (2001)*, The macro economic evaluation model (MEEM): An approach to priority setting in health care*. A thesis submitted for the degree of Doctor of Philosophy, Department of Management: Monash University.

Carter, S. M. and Little, M. (2007), Justifying knowledge, justifying method, taking action: Epistemologies, methodologies, and methods in qualitative research. *Qualitative Health Research* Vol 17 No. 10, pp.1316-1328.

Carpenter, G. (1986), Cash flow management in government*, Australian Accountant,* June, pp. 37-40.

Cassileth, B.R., Lusk, E.J., Miller, D.S., and Hurwitz, S. (1982), Attitudes towards clinical trials among patients and the public. *Journal of the American Medical Association,* Vol 248, pp. 968–970.

Cavana, R.Y., Delahaye, B.L. and Sekaran, U. (2001), *Applied business research: qualitative and quantitative methods*. Queensland: John Wiley & Sons, Ltd.

Chaiken, B. P. (2003), Clinical technology: Are you getting your money's worth? *Healthcare Financial Management,* Vol 57, No.2, pp. 66-69.

Chalkidou, K., Culyer, A., Naidoo, B. and Littlejohns, P. (2008), Cost-effective public health guidance: Asking questions from the decision-maker's viewpoint. *Health Economics* Vol 17 No.3, pp. 441-448.

Chapman, C. S., Hopwood, A.G. and Shields, M. D. (2006), *Handbook of Management Accounting Research Volume 1*. Elsevier.

Chapman, C. S., Hopwood, A.G. and Shields, M. D. (2007), *Handbook of Management Accounting Research Volume 2*. Elsevier.

Chapman, C. S., Hopwood, A.G. and Shields, M. D. (2009), *Handbook of Management Accounting Research Volume 3*. Elsevier.

Christie, D. R. H., Gabriel, G. S., and Dear, K. (2007), Adverse effects of a multicentre system for ethics approval on the progress of a prospective multicentre trial of cancer treatment: How many patients die waiting? *Internal Medicine Journal,* Vol 37, pp. 680–686.

Chua, F. W. (1995), Experts, networks and inscriptions in the fabrication of accounting images: A story of the representation of three public hospitals. *Accounting Organizations and Society*. Vol. 20. No. 213. pp. 11 l-145.

Chua, F. W. and Preston, A. (1994), Worrying about accounting in health care. *Accounting, Auditing & Accountability Journal*, Vol. 7 No. 3, pp. 4-17.

Clarke, P., Gray, A. and Holman, R. (2002), Estimating utility values for health states of type 2 diabetic patients using the EQ5D (UKPDS 62). *Medical Decision Making* Vol 22 No. 4, pp. 340 – 349.

Clarkson, M.B.E, (1995). A stakeholder framework for analyzing and evaluating corporate social performance, *Academy of Management Journal,* Vol.20, No. 1, pp.92-118.

Cleverly, W.O. and Harvey, R.K. (1992), Is there a link between hospital profit and quality? *Healthcare Financial Management*, Vol. 46 No. 9, pp. 40-5.

Clinical Trials Transformation Initiative. (2009), *Approved project concepts*. Retrieved 29 March, 2009, from https://www.trialstransformation.org/projects/approved-project-concepts/

Coast, J., Smith, R. D. and Lorgelly, P. (2008), Welfarism, extra-welfarism and capability: The spread of ideas in health economics. *Social Science & Medicine* Vol 67, pp.1190–1198.

Collier, P. (2008), Stakeholder accountability: A field study of the implementation of a governance improvement plan. *Accounting, Auditing &Accountability Journal* Vol. 21 No. 7, pp. 933-954.

Collier, R. (2009a), Rapidly rising clinical trial costs worry researchers. *Canadian Medical Association Journal,* Vol 180 No. 3, pp. 277-278.

Collier, R. (2009b), Drug development cost estimates hard to swallow. *Canadian Medical Association Journal,* Vol 180 No. 3, pp. 279-280.

Collis, D.J. and Montgomery, C.A. (1997), *Corporate strategy: Resources and the scope of the firm,* McGraw-Hill, Chicago, IL.

Comanora, W. S. and Schweitzer, S. O. (2007), Determinants of drug prices and expenditures. *Managerial and Decision Economics,* Vol 28, pp. 357–370.

www.interscience.wiley.com) DOI: 10.1002/mde.1346

Commonwealth of Australia (2006), *Handbook of cost benefit analysis*, January 2006. Accessed 16 February 2008 from http://www.finance.gov.au/obpr/cost-benefit-analysis.html

Coney, S. (1988), *The unfortunate experiment*. Auckland: Penguin.

Cook, J., Drummond, M. and Heyse, J.F. (2004), Economic endpoints in clinical trials. *Statistical Methods in Medical Research*, Vol 13, pp. 157-176.

Cookson, R. (2003), Willingness-to-pay methods in health care: a sceptical view. *Health Economics* Vol 12 pp. 891–894.

Cornell, B. and Shapiro, A.C. (1987) Corporate Stakeholders and Corporate Finance, *Financial Management,* Vol 16, pp. 5-14.

Condon, J. and Goldstein, J. (1998), Value based management - the only way to manage for value. *Accountancy Ireland,* Vol 30 No. 5, pp.10-12. http://ezproxy.utas.edu.au/login?url=http://search.proquest.com/docview/223178960?accountid=14245

Cordery, C., Baskerville, R and Porter, B. (2010), Control or collaboration? Contrasting accountability relationships in the primary health sector. *Accounting, Auditing & Accountability Journal* Vol. 23 No. 6, 2010 pp. 793-813

Coster, G. D. (2011), *The National Health Board in New Zealand: delivering better, sooner more convenient healthcare.* The Nuffield Trust: London.

Cotton, P., Fraser, I. and Hill, W. Y. (2000). The social audit agenda. *International Journal of Auditing,* Vol 4, pp. 3-28.

Counties Manukau District Health Board (2008), Annual Report as at 30 June 2008. available at: http://www.pdfdownload.org/pdf2html/pdf2html.php?url=http%3A%2F%2Fwww%2Ecmdhb%2Eorg%2Enz%2Fabout%5Fcmdhb%2FPlanning%2FResearch%2FCMDHB%2Dresearch%2Dstrategy%2Epdf&images=no accessed 22 November 2009

Counties Manukau District Health Board (2009a), Health Research Strategy for Counties Manukau District CMDHB. available at: http://www.pdfdownload.org/pdf2html/pdf2html.php?url=http%3A%2F%2Fwww%2Ecmdhb%2Eorg%2Enz%2Fabout%5Fcmdhb%2FPlanning%2FResearch%2FCMDHB%2Dresearch%2Dstrategy%2Epdf&images=no accessed 22 November 2009

Counties Manukau District Health Board (2009b), Annual Report as at 30 June 2009. available at: http://www.pdfdownload.org/pdf2html/pdf2html.php?url=http%3A%2F%2Fwww%2Ecmdhb%2Eorg%2Enz%2Fabout%5Fcmdhb%2FPlanning%2FResearch%2FCMDHB%2Dresearch%2Dstrategy%2Epdf&images=no accessed 22 November 2009

Counties Manukau District Health Board. (n.d.), About Counties Manukau District Health Board. Retrieved 1 June 2008 www.cmdhb.org.nz/Counties/About_CMDHB

Cox, K. (1999), Researching research: patient's experiences of participation in phase I and II ant-cancer drug trials. *European Journal of Oncology Nursing,* Vol 3, pp. 143–152.

Cox, K. (2002), The hopes of the dying: Examining patients' experience of participation in early phase cancer clinical trials. *Nursing Times Research,* Vol 7 No. 1 pp. 60-74.

Cox, K. (2003), Assessing the quality of life of patients in phase I and II anti-cancer drug trials: Interviews versus questionnaires. *Social Science and Medicine* Vol 56 No 5, pp. 921-934

Creswell, J.W. (1994), *Research design: Qualitative and quantitative approaches*. Thousand Oaks, CA: Sage.

Creswell, J.W. (2003), *Research design: Qualitative, quantitative and mixed methods approaches* (2nd edition) Thousand Oaks, CA: Sage.

Creswell, J. W. (2008), The selection of a research design. Accessed 10/3/2012 from http://www.sagepub.com/upm-data/27395_Pages5_11.pdf

Creswell, J.W. and Plano Clark, V.L. (2007), Designing and Conducting Mixed Methods Research. Thousand Oaks, CA: Sage.

Culyer, A. J. (1985), *Economics*. Oxford: Blackwell.

Culyer, A. J. (1989), The normative economics of health care finance and provision. *Oxford Review of Economic Policy,* Vol 5 No. 1, pp.34–56.

Culyer, A. J. (2006), The bogus conflict between efficiency and vertical equity. *Health Economics*, Vol 15 No. 11, pp.1155-1158.

Curry, L. A., Nembhard, I. and Bradley, E. H. (2009), Qualitative and mixed methods provide unique contributions to outcomes research. *Circulation American Heart Foundation* Vol 119 No.10, pp. 1442-1452.

Daniels, A. (2004), Listening to New Zealand nurses. A survey of intent to leave, job

satisfaction, job stress and burnout. *Department of Health Sciences: Auckland University of Technology*

Davila, A. and Foster, G. (2007), Management control systems in early-stage startup companies, *The Accounting Review*, Vol 82 No. 4, pp. 907-37.

Davis, A.M., Hull, S. C., Grady, C., Wilfond, B.S. and Henderson, G. (2002), The invisible hand in clinical research: The study coordinator's critical role in human subject protection. *The Journal of Law, Medicine and Ethics;* Vol 30, No. 3, pp. 411-419.

Deegan, C. (2002), Introduction: The legitimising effect of social and environmental disclosures - a theoretical foundation. *Accounting, Auditing & Accountability Journal*, Vol. 15 No. 3, pp. 282-311

Denzin, N. and Lincoln, Y. (2005), *Handbook of Qualitative Research*. (3rd ed). Thousand Oaks California: Sage.

DePoy, E., and Gitlin, L. N. (1994), *Introduction to research: Multiple strategies for health and human services*. St. Louis, MO: C. V. Mosby.

Dev, A., Kauf, T., Zeky, A., Patel, K., Heller, K. Schulman, K. and McHutchison, J. (2008), Factors influencing the participation of gastroenterologists and hepatologists in clinical research. *BMC Health Services Research*, Vol 8 No 208. *Accessed 1/12/2009* from: http://www.biomedcentral.com/1472-6963/8/208

DeVries, J. H., Snoek, F.J., Kostense, P. J. and Heine, R. J. (2003), Improved glycaemic control in type I diabetes patients following participation per se in a clinical trial mechanisms and implications. *Diabetes/Metabolism Research and Reviews,* Vol 19 No 5, pp. 357-362.

Dey, C. R. (2000), Bookkeeping and ethnography at Traidcraft plc: a review of an experiment in social accounting. *Social and Environmental Accounting Journal*, Vol 20 No. 1, pp.16–19.

DiCicco-Bloom, B. and Crabtree, B. F. (2006), The qualitative research interview. *Medical Education*, Vol 40, pp.314–321

DiMasi, J.A. (2002), The value of improving the productivity of the drug development process: faster times and better decisions. *PharmacoEconomics* Vol 20 Suppl. No.3, pp. 1-10.

DiMasi, J. A. (2008), The economics of new drug development: Costs risks and returns. Paper

presented to *The New England Drug Metabolism Group Spring Meeting*. Cambridge, MA. March 12. Accessed from 12 August 2009 *units.sla.org/division/dpht/meetings/spring2007/dimasi_2007s.ppt*

DiMasi, J. A., Grabowski, H. and Vernon, J. (1995), R&D costs, innovative outputs and firm size in the pharmaceutical industry. *International Journal of the Economics of Business,* Vol 2 No. 2, pp. 201-219.

DiMasi, J. A., Grabowski, H. and Vernon, J. (2004), R&D Costs and returns by therapeutic category. *Drug Information Journal,* Vol 38, pp. 211–223.

DiMasi J.A., Hansen RW, and Grabowski H.G. (2003), The price of innovation: New estimates of drug development costs. *Journal of Health Economics,* Vol 22, pp.151-185.

DiMasi, J. A., Hansen, R.W., Grabowski, H.G. and Lasagna, L. (1995), Research and development costs for new drugs by therapeutic category. A study of the US pharmaceutical industry. *PharmacoEconomics*, Vol 7 No. 2, pp. 152-169.

Dix Smith, M., Berger, M., Bingefors, K., Hedblom, E., Pashors, C. and Torrance, G. (2003), *Health care cost, quality and outcomes: ISPOR book of terms,* Lawrenceville, NJ: International Society of Pharmacoeconomics and Outcomes Research.

Dobb, M. (1973), *Theories of value and distribution since Adam Smith: Ideologies and economic theory*. New York and London: Cambridge University Press.

Dobes, L. (2007). *A century of Australian cost-benefit analysis*. Canberra, Australia, Office of Best Practice Regulation, Department of Finance and Deregulation. http://www.finance.gov.au/obpr/docs/Working-paper-1-Leo-Dobes.pdf

Dolan, P. (2000), The measurement of health-related quality of life. *Handbook of Health Economics*, pp. 1723-1755. Culyer AJ, Newhouse JP, eds. Amsterdam: Elsevier

Dolan P, Gudex, C., Kind, P. and Williams A. (1995), *A social tariff for EuroQol: results from a UK general population survey.* Discussion paper no. 138. Centre for Health Economics, University of York. Retrieved 19 September 2010 from http://ideas.repec.org/p/chy/respap/138chedp.html

Donaldson, T., and Preston, L. E. (1995), The stakeholder theory of the corporation: concepts, evidence, and implications. *Academy of Management Review,* Vol 20 No.1, pp.63-91.

Donovan, J. L., Brindle, L. and Mills, N. (2002), Capturing users' experiences of participating in cancer trials. *European Journal of Cancer Care,* Vol 11, pp. 210-214.

Dopfer, K; Foster, J. and Potts, J. (2004), Micro–meso–macro. *Journal of Evolutionary Economics*. Vol 14, pp. 263–279.

Doyle, l., Brady, A. and Byrne, G. (2009), An overview of mixed methods research. *Journal of Research in Nursing*; Vol 14 No.2, pp. 175-185.

Doz, Y. L. and Hamel, G. (1998). *Alliance Advantage: The Art of Creating Value Through Partnering* (First ed.). Boston: Harvard Business School Press.

Drummond, M.F., O'Brian, B., Stoddart, G.L. and Torrance, G.W. (2000), *Methods for the economic evaluation of health care programmes,* 2nd ed. N.Y, Oxford Press.

Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brian, B., and Stoddart, G.L., (2005), *Methods for the economic evaluation of health care programmes,* 3rd ed. N.Y, Oxford Press.

Easterby-Smith, M., Thorpe, R. and Lowe, A. (1991), *Management research: An introduction*. London: Sage.

Edwards, S. J., Lilford, R. J. and Hewison, J. (1998), The ethics of randomised controlled trials from the perspectives of patients, the public, and healthcare professionals. *British Medical Journal,* Vol 317 pp.1209-1212.

Ellis, P. M. (2000), Attitudes towards and participation in randomised clinical trials in oncology: A review of the literature. *Annals of Oncology,* Vol 11, pp. 939-945.

Emanuel, E., Schnipper, L., Kamin, D., Levinson, J. and Lichter, A. (2003), The costs of conducting clinical research. *Journal of Clinical Oncology*, Vol 21 No. 22, pp. 4145-4150.

Este, R. (1976), *Corporate social accounting.* John Wiley & Sons. New York. NY

Evan, W. F. and Freeman, R. E. (1993) In *Ethical Theory and Business* (Eds, Beauchamp, T. and Bowie, N.) Prentice Hall, Englewood Cliffs, N.J., pp. 75-84.

Evans, W., Dahrouge, S., Stapleton, J., Quinn, C., Pollock, D., Waterfield, B., Lister, D., Hansel, F. and Smith, A. (2000), An estimate of the cost of conducting phase II trials in lung cancer. *Lung Cancer,* Vol 28 No.2, pp. 85-95.

Fallowfield, L.J. (1995), Can we improve the professional and personal fulfillment of doctors in cancer medicine? *British Journal of Cancer,* Vol 71, pp. 1132-1133.

Featherstone, K. and Donovan, J.L. (1998), Random allocation or allocation at random? Patients'

perspectives of participation in a randomized controlled trial. *British Medical Journal,* Vol 317, pp. 1177-1180.

Ferreira, L.D. and Merchant, K.A. (1992), Field research in management accounting and control: a review and evaluation, *Accounting, Auditing & Accountability Journal*, Vol. 5 No. 4, pp. 3-34.

Finkler, S. A., Henley, R. J. and Ward, D. M. (2003), Evidence-based financial management. *Healthcare Financial Management* Vol 57, No. 10, pp. 64-68.

Fireman, B., Fehrenbacher, L., Gruskin, E. and Ray, G.T. (2000), Cost of care for patients in cancer clinical trials. *Journal of the National Cancer Institute,* Vol 92 No. 2 pp. 136-142.

Flagler, B. (2005), Exposing the myth *Unlimited Magazine, September*.

Foëx, B. A. (2008), The ethics of clinical trials. *Anaesthesia and Intensive Care Medicine,* Vol 10 No.2 pp. 98-101.

Forge, S. (2009), Forecasting quantitatively using micro/meso/macro-economics with scenarios for qualitative balance. *Foresight* Vol 11 No. 1, pp. 43-60.

Freeman, R. E. (1983). Strategic management: a stakeholder approach. In R. Lamb (Ed.), *Advances in strategic management* Vol. 1, pp. 31-60. Greenwich, CT: JAI.

Freeman, R, E. (1984), *Strategic management: A stakeholder approach,* Boston, Mass. Pitman.

Freeman, R. E. (1999), Divergent stakeholder theory. *Academy of Management Review,* Vol 24 No.2, pp. 233-236.

Friedman, A, and Miles, S. (2002), Developing stakeholder theory. *Journal of Management Studies* Vol39 No.1, pp. 1-21.

Freyens, B. (2008), Macro-, Meso- and Microeconomic considerations in the delivery of social services. *International Journal of Social Economics,* Vol 35 No. 11, pp. 823-845.

Frooman, J. (1999), Stakeholder Influence Strategies. *Academy of Management Review* Vol 24 No.2 pp.191-205.

Funding First (2000). *Exceptional returns: the economic value of America's investment in medical research*. New York (NY): The Lasker Foundation.

Gale, E.A., Beattie, S.D., Hu, J., Koivisto, V. and Tan M. H. (2007), Recruitment to a clinical trial improves glycemic control in patients with diabetes. *Diabetes Care,* Vol 30, No 12, pp. 2989-2992.

Getz, K. A. (2007a), Drowning in the sea of regulatory compliance. *Applied Clinical Trials*, Feb, pp. 1-3

Getz, K. A. (2007b), Industry trials poised to win back academia. *Applied Clinical Trials,* April, pp. 1-3.

Getz, K.A. (2008a), Protocol design trends and their effect on clinical trial performance. *The Regulatory Affairs Journal Pharma, May*, Retrieved 20 March 2009 from http://www.rajpharma.com/search?mode=results&queries_search_query=getz

Getz, K. A. (2008b), In search of efficiency between trial phases. *Applied Clinical Trials, March*, pp. 1-3

Getz, K. A. (2008c), Is investigative site feasibility feasible? *Applied Clinical Trials, July*, pp. 1-3

Getz, K. A. (2009), Burying sites under safety reporting. *Applied Clinical Trials, Jan*, pp.1-2

Getz, K. A.; Wenger, J.; Campo, R.; Seguine, Edward S. M. and Kaitin, K. (2008), Assessing the impact of protocol design changes on clinical trial performance. *American Journal of Therapeutics.* Vol 15 No. 5, pp.450-457.

Ghonkrokta, S. S., and Lather, A. (2007). Identification of role of social audit by stakeholders as accountability tool in good governance *Journal of management research*, Vol 7 No. 1, pp. 18-26.

Giaccotto, C., Sonterre, R.E. and Vernon, J. A. (2005), Drug prices and research and development investment behavior in the pharmaceutical industry. *Journal of Law and Economics* XLVIII. Retrieved 14 Dec 2009 from http://ideas.repec.org/a/ucp/jlawec/y2005v48i1p195-214.html

Giddings, L. S. (2006), Mixed-methods research: Positivism dressed in drag? *Journal of Research in Nursing*, Vol 11 No. 3, pp. 195-203.

Gilgun, J. (2010). Reflexivity and qualitative research. *Current Issues in Qualitative Research,* Vol 1 No. 2, pp. 1-8.

Giuliano, A. R., Mokuau, N., Hughes, C., Tortolero-Luna, G., Risendal, B., Ho, R. C. S., McCaskill, Stevens, W. and Prewitt, T. E. (2000), Participation of minorities in cancer research: the influence of structural, cultural, and linguistic factors, *Annals of Epidemiology,* Vol 10 No. 8 (Suppl) pp. S22 34.

Glass, H. and DiFrancesco, J. (2007), Understanding site performance differences in multinational phase III clinical trials. *International Journal of Pharmaceutical Medicine,* Vol 21, No 4, pp. 279-286.

Golafshani, N. (2003), Understanding reliability and validity in qualitative research. *The Qualitative Report,* Vol 8 No.4, pp.597-607. Available at http://www.nova.edu/ssss/QR/QR8-4/golafshani.pdf

Gold, M. R., Siegel, J. E., Russell, L. B. and Weinstein, M. C. (1996), *Cost-effectiveness in health and medicine.* New York: Oxford University Press.

Goldman, D., Berry, S., McCabe, M., Kilgore, M., Potosky, A.; Schoenbaum, M., Schonlau, M., Weeks, J., Kaplan, R. and Escarce, J. (2003), Incremental treatment costs in national cancer institute–sponsored clinical trials. *Journal of the American Medical Association,* Vol 289 No. 22, pp.2970-2977.

Goldman, D., Schoenbaum, M., Potosky, A., Weeks, J., Berry, S., Escarce, J., Weidmer, B., Kilgore, M., Wagle, N., Adams, J., Figlin, R., Lewis, J., Cohen, J., Kaplan, R. and McCabe, M. (2001), Measuring the Incremental Cost of Clinical Cancer Research. *Journal of Clinical Oncology,* Vol19 No. 1, pp.105-110.

Grady, C and Edgerly, M (2009), Science, technology and innovation: Nursing responsibilities in clinical research. *Nursing Clinics of North America,* Vol 44 No. 4, pp. 471- 481.

Grafton, J., Lillis, A. M. and Mahama, H. (2011), Mixed methods research in accounting. *Qualitative Research in Accounting & Management*. Vol. 8 No. 1, pp. 5-21.

Graham, J.R., Harvey, C.R. and Rajgopal, S. (2005), The economic implications of corporate financial reporting, *The Journal of Accounting and Economics*, Vol. 40 No's 1-3, pp. 3-73.

Gramlich, E. M. (1981), *Benefit-cost analysis of government programs*. New Jersey, USA, Prentice-Hall.

Gramlich, E. M. (2002), The methodology of benefit-cost analysis: Avoiding politics in decision making. *Vital Speeches of the Day,* Vol 69 No.3, pp. 68-75.

Gray, J. A. M. (2011), *How to get better value health care: Asia Pacific Edition*. Oxford: Offox Press.

Gray, J. A. M. (2007), *How to get better value health care.* Oxford: Offox Press.

Gray, R. H. (2000), Current developments and trends in social and environmental auditing,

reporting and attestation: a review and comment. *International Journal of Auditing*, Vol 4, No. 3, pp. 247–268.

Gray, R. H. (2001), Thirty years of social accounting, reporting and auditing: What (if anything) have we learnt? *Business Ethics: A European Review*, Vol 10, No. 1, pp. 9–15.

Gray, R. H. (2002), The social accounting project and Accounting, Organizations and Society: Privileging engagement, imaginings, new accountings and pragmatism over critique? *Accounting, Organizations and Society*, Vol. 27 No. 7, pp. 687-708.

Gray, R H. (2006), Social, environmental and sustainability reporting and organisational value creation? Whose value? Whose creation? *Accounting, Auditing & Accountability Journal* Vol. 19 No. 6, pp. 793-819.

Gray, R., Collison, D. and Bebbington, J. (1998), Environmental and social accounting and reporting, in *Financial Reporting Today: Current and Emerging Issues*, Institute of Chartered Accountants in England and Wales (ICAEW), London.

Gray, R, Dillard, J. And Spence, C. (2009), Social accounting research as if the world matters, *Public Management Review*, 11: 5, 545-573.

Gray, R., Kouhy, R. and Lavers, S. (1995a), Constructing a research database of social and environmental reporting by UK companies: A methodological note, *Accounting, Auditing & Accountability Journal*, Vol. 8 No 2, pp. 78-101.

Gray, R.H., Kouhy, R. and Lavers, S. (1995b), Corporate social and environmental reporting: a review of the literature and a longitudinal study of UK disclosure, *Accounting, Auditing & Accountability Journal,* Vol. 8 No. 2, pp. 47-77

Gray, R., Owen, D., Adams, C. (1996), *Accounting and Accountability: Changes and Challenges in Corporate and Social Reporting*, Prentice Hall, London.

Greene, J.C. (2005), The generative potential of mixed methods inquiry. *International Journal of Research Method in Education,* Vol 28 No.2, pp. 207–211.

Greene, J. C., Caracelli, V. J. and Graham, W. F. (1989), Toward a conceptual framework for mixed method evaluation designs. *Educational Evaluation and Policy Analysis,* Vol 11, pp. 255–274.

Grocott, R., Schoeler, R., Priest, V., Hall, C., Scott, G., Hansen, P. and Wilkenson, B. (2007), *Prescription for pharmacoeconomic analysis: Methods for cost-utility analysis* Wellington: PHARMAC

Guest, G., Bunce, A. and Johnson, L. (2006), How many interviews are enough? An experiment with data saturation and variability. *Field Methods*, Vol 18 No. 1, pp. 59-68.

Guthrie, J. and Parker, L.D. (1990), Corporate social disclosure practice: a comparative international analysis, *Advances in Public Interest Accounting*, Vol. 3, pp. 159-76.

Gutman, J. (1982), A means-end chain model based on consumer categorization processes. *Journal of Marketing*, Vol 46, pp.60-72.

Gutman, J. (1990), Adding meaning to values by directly assessing value-benefit relationships. *Journal of Business Research*, Vol 20, pp.153-160.

Hage, J. (2009), Meso-level metrics for impact: Metrics for the treatment or meso-level of the Canadian health care system in Canadian Academy of Health Sciences *In: Return on investments in health research*. Ottawa (ON): Canadian Academy of Health Sciences; pp. A42–74. Accessed 21 January 2010 from www.cahsacss.ca/e/assessments/completedprojects.php.

Hall, B. and Howard, K. (2008), A synergistic approach: Conducting mixed methods research with typological and systemic design considerations. *Journal of Mixed Methods Research*; Vol 2, pp.248 -270.

Hammond, M. and Wiriyapinit, M. (2005), Learning through online discussion: a case of triangulation in research, *Australasian Journal of Educational Technology*, Vol 21 No. 3, pp. 283-302.Hanley B., Truesdale A., King A., Elboure D. & Chalmers I. (2001), Involving consumers in designing, conducting and interpreting randomised controlled trials: questionnaire survey. *British Medical Journal* Vol 322, pp.519–523.

Hanley, N. and Spash, C. L. (1993), *Cost-Benefit Analysis and the Environment.* Aldershot: Edward Elgar.

Hanney, S., Grant, J., Wooding, S. and Buxton, M. (2004), Proposed methods for reviewing the outcomes of health research: The impact of funding by the UK's 'arthritis research campaign'. *Health Research Policy and Systems,* Vol 2 No.4, Retrieved 12 July 2009 from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC503400/?tool=pubmed

Hanson, E., Magnusson, L., Nolan, J. and Nolan, M. (2006), Developing a model of participatory research involving researchers, practitioners, older people and their family carers: An international collaboration. *Journal of Research in Nursing,* Vol 11 No.4, pp. 325–342.

Hart, S. L. and Sharma, S. (2004), Engaging fringe stakeholders for competitive emagination. *Academy of Management Executive.* Vol 18, No.1, pp. 7-18.

Hartman, E. (2011), Virtue, profit, and the separation thesis: An Aristotelian view. *Journal of Business Ethics*, Vol.99, No.1, pp. 5-17.

Heald, D. (2002), Value for money tests and accounting treatment in PFI schemes. *Accounting, Auditing & Accountability Journal,* Vol 16, No. 3, pp. 342-371.

Health Research Council of New Zealand (2002), *Guidelines on Ethics for Health Research.* Accessed 2 March 2008 from http://www.hrc.govt.nz/root/Ethics/Ethics%20Overview/HRC_Guidelines_on_Ethics_in_Health_Research.html

Health Research Council of New Zealand (2004), *Biomedical and clinical research outcomes evaluation.* Accessed 12 Nov 2009 from http://www.hrc.govt.nz/

Health Research Council of New Zealand (1995), *Guidelines on Ethics in Health Research.* Accessed 12 Nov 2009 from http://www.hrc.govt.nz/

Helman, S. (1979), Editorial: Randomized clinical trials and the doctor-patient relationship. *Cancer Clinical Trials* Vol 2, pp. 189-193

Henzlova, M.J., Blackburn, G.H., Bradley, E.J. and Rogers, W.J. (1994), Patient perception of a long-term clinical trial: Experience using a close-out questionnaire in the Studies of Left Ventricular Dysfunction (SOLVD) trial. *Controlled Clinical Trials,* Vol 15 No.4, pp. 284-293.

Hicks, C. (1996), Nurse researcher: A study of a contradiction in terms. *Journal of Advanced Nursing,* Vol 24, pp. 357-363.

Hicks, J. R. (1939), The foundations of welfare economics. *Economic Journal*, Vol 49, pp.696–712. Published by: Blackwell Publishing for the Royal Economic Society Stable URL: http://www.jstor.org/stable/2225023 Accessed: 08/02/2010

Hicks, J. R., (1946), *Value and Capital* (2nd edition); London: Oxford University Press.

Hill, C. W. L. and Jones, J. M. (1992), Stakeholder Agency Theory, *Journal of Management Studies*, Vol. 29, No. 2, pp. 131-154.

Hill, W. Y., Fraser, I. and Cotton, P. (2001). On patients' interests and accountability: Reflecting on Some dilemmas in social audit in primary health care. *Critical Perspectives on Accounting* Vol. 12, pp. 453–469.

Hiltner, A. A. (1975). *An inquiry into the future of current value accounting.* The University of Nebraska- Lincoln). *ProQuest Dissertations and Theses*, p.246 http://ezproxy.utas.edu.au/login?url=http://search.proquest.com/docview/288005476?accountid=14245

Hoffman, D. M. (2009), Multiple methods, communicative preferences and the incremental interview approach protocol. *Forum Qualitative Sozialforschung / Forum: Qualitative Social Research,* Vol 10 No.1, Art. 41, Accessed 12 November 2009 *http://nbn-resolving.de/urn:nbn:de:0114-fqs0901419*.

Holcombe, R. G. (2011), Pluralism and heterodoxy in economic methodology. *The Review of Austrian Economics.* Vol. 24, pp.57–65.

Hopwood, A.G. (1984), Accounting and the pursuit of efficiency, in Hopwood, A.G. and Tomkins, C. (Eds), *Issues in Public Sector Accounting*, Philip Allan Publishers, London, pp. 187-97.

Hopwood, A.G. (1990), Accounting and organisational change. *Accounting, Auditing & Accountability Journal,* Vol 3 No 1, pp.7–17.

Hopwood, A.G. (1992), Accounting calculation and the shifting sphere of the economic, *European Accounting Review*, Vol. 1, pp. 125-43.

House of Commons Health Committee (2005), *The influence of the pharmaceutical industry* (Fourth Report for Session 2004–5). London: The Stationary Office Ltd. Accessed 15/2/2010 from http://www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/4202.htm

Howard, J. C. (1977), *Consumer Behaviour: Application of Theory* New York: McGraw-Hill.

Huang, E.S., Brown, S. E., Ewigman, B.G., Foley, E.C. and Meltzer, D.O. (2007), Patient perceptions of quality of life with diabetes-related complications and treatments. *Diabetes Care*. Vol 30 No. 10, pp. 2478-2483.

Hudson, M. (2004), He Matatika Maori, Maori and ethical review in Health Research, Auckland University of Technology: Auckland.

Hull, C. L. (1944), Value, valuation, and natural-science methodology. *Philosophy of Science*, Vol. 11, No. 3, pp. 125-141. Published by: The University of Chicago Press on behalf of the Philosophy of Science Association Stable URL: http://www.jstor.org/stable/184602. Accessed: 25/12/2011 23:09

Hunt, S.M. and McEwen, J. (1980), The development of a subjective health indicator, *Sociology of Health and Illness* Vol 2 No. 3, pp.231–246.

Hussain-Gambles M. (2004), South Asian patients' views and experiences of clinical trial participation. *Family Practice,* Vol 21 No. 6, pp. 636-642.

Hussey, J. and Hussey, R. (1997), *Business research: A practical guide for undergraduate and postgraduate students*. New York: Palgrave.

Hybels, R. C. (1995), On legitimacy, legitimation, and organizations: A critical review and integrative theoretical model, *Academy of Management Journal, Special Issue: Best Papers Proceedings*, *1995*, pp. 241 - 245.

Hyden, L.C. and Bulow, P.H. (2003). Who's talking: drawing conclusions from focus groups – some methodological considerations. *International Journal of Social Research Methodology* Vol 6, pp. 305–321

Hynes, D., Reda, D., Giobbie-Hurder, A., Abdellatif, M., Weinberger, M., Oddone, E., Wasson, J. and Henderson, W. (1999), Measuring costs in multisite randomized controlled trials: Lessons from the VA cooperative studies program. *Medical Care,* Vol 37 No. 4, VA Supplement, AS27-36.

International Review Board (nd), *The Belmont Report*. Accessed 8 June 2011 from www.uwrf.edu/grants/IRB/BelmontReport.pdf

Ireland, J., Tambyah, M. M., Neofa, Z. and Harding, T. (2008), The tale of four researchers: Trials and triumphs from the phenomenographic research specialization. In: AARE 2008 International Education Conference: Changing Climates: Education for Sustainable Futures, 30th November - 4th December2008, Queensland University of Technology, Brisbane.

Ittner, C.D. and Larcker, D.F. (2001), Assessing empirical research in managerial accounting: a value-based management perspective, *Journal of Accounting and Economics*, Vol. 32 No's 1/3, pp. 349-410.

Jenkins, R.R., N. Owens and L.B. Wiggins (2001), Valuing reduced risks to children: The case of bicycle safety helmets, *Contemporary Economic Policy,* Vol. 19, No. 4, pp. 397-408.

Jensen, M. C. (2002). Value maximization, stakeholder theory, and the corporate objective function. *Business Ethics Quarterly* Vol.12, No.2, pp. 235-56.

Johannesson, M. and Johannesson, B. (1991), Economic evaluation in health care: is there a role for cost-benefit analysis? Health Policy, Vol 17, pp. 1-23.

Johns, M. M., Barnes, M. and Florencio, P. S. (2003), Restoring balance to industry-academia relationships in an era of institutional conflicts of interest: Promoting research while maintaining trust. *Journal of the American Medical Association,* Vol 289 No.6, pp.741-746

Johnson, R. B. and Onwuegbuzie, A. J. (2004), Mixed methods research: A research paradigm whose time has come. *Educational Researcher*; Vol 33, pp. 14-26.

Johnston, S. C. (2007), Clinical trials: Rising costs limit innovation. *Annals of Neurology,* Vol 62 No. 6, pp. A 6 -7.

Jones, T. M., and Wicks, A. C. (1999), Convergent stakeholder theory. *Academy of Management Review,* Vol 24 No.2, pp. 206- 221.

Jull, A., Wills, M., Scoggins, B. and Rodgers, A. (2005), Clinical trials in New Zealand – Treading water in the knowledge wave? *New Zealand Medical Journal,* Vol 118 No.1221. Accessed 12 November 2009 from http://www.nzma.org.nz/journal/1181221/1638/content.pdf

Kaitin, K. (2003), CROs provide gateway to worldwide clinical trial recruitment efforts. *Tufts CSDD Impact Report,* Vol 5 No. 4, July/August.

Kaitin, K. (2005), Growing protocol design complexity stresses investigators, volunteers *Tufts CSDD Impact Report,* Vol 7 No 6, Nov/Dec.

Kaitin, K. (2006), New drugs entering clinical testing in top 10 firms jumped 52% in 2003-05 *Tufts CSDD Impact Report,* Vol 8 No.3, May/June.

Kaitin, K. (2008), Growing protocol design complexity stresses investigators, volunteers. *Tufts CSDD Impact Report,* Vol.10 No. 1, Jan/Feb.

Kandzari, Roe, Chen, Lytle, Pollack, Harrington, Ohman, Gibler and Peterson (2005), Outcomes, health policy, and managed care - influence of clinical trial enrollment on the quality of care and outcomes for patients with non-st-segment elevation acute coronary syndromes. *American Heart Journal,* Vol 149 No.3, pp.474-481.

Ketley, D. and Woods, K.L. (1993), Impact of clinical trials on clinical practice: Example of thrombolysis for acute myocardial infarction. *Lancet,* Vol 342, pp.891-945.

Kind, P. Lafata, J. E., Matuszewski, K and Raisch, D. (2010), The use of QALYs in clinical and

patient decision-making: Issues and prospects. *Value in Health,* Vol 12 Sup 1 pp.27-30

Kitson, A. (2002), Recognising relationships: reflections on evidence-based practice. *Nursing Inquiry,* Vol 9 No.3, pp. 179–186.

Kochan, T. A. and Rubinstein, S. (2000), Toward a stakeholder theory of the firm: The Saturn Partnership, *Organization Science*, Vol 11 No. 4 pp. 367-386.

Krueger, R. A. (1995), The future of focus groups. *Qualatative Health Research*; Vol 5, pp. 524-530

LaFleur, J., Tyler, L.S. and Sharma, R.R. (2004), Economic benefits of investigational drug services at an academic institution. *American Journal of Health System Pharmacy*. Vol 61 No.1, pp.27-32.

Lantos, J. (1993), Informed consent? The whole truth for patients. *Cancer,* Vol 72, pp. 2811–2815.

Lawrence, S., Alam, M., Northcott, D. and Lowe, T. (1997), *Accounting, Auditing & Accountability Journal*, Vol. 10 No. 5, pp. 665-683.

Lee, J. and Breaux, S. (1983), Accrual of radiotherapy patients to clinical trials. *Cancer,* Vol 52, pp. 1014-1016.

Lee, S. (1999), The crisis in clinical research. *Journal of the American Medical Association*. Vol 282 No. 20, pp.1913-1916.

Lehman, G. (1995), A legitimate concern for environmental accounting, *Critical Perspectives on Accounting*, Vol. 6, pp. 393-412.

Lehman, G. (1999), Disclosing new worlds: a role for social and environmental accounting and auditing, *Accounting, Organizations and Society*, Vol. 24, pp. 217-41.

Lehman, G. (2001), Reclaiming the public sphere: problems and prospects for corporate social and environmental accounting, *Critical Perspectives on Accounting*, Vol. 12, pp. 713-33.

Lenman, J. (2000), Preferences in their place. *Environmental Values,* Vol 9 No.4, pp.431-451.

Lepak, D. P., Smith, K. G., Taylor, M. S. (2007), Value creation and value capture: A multilevel perspective. *Academy of Management Review* Vol 32 No.1, pp. 180-194.

Lichtenberg, F. R, (2007), Benefits and costs of newer drugs: An update. *Managerial and Decision Economics*, Vol 28, pp. 485–490.

Light, D.W. and Lexchin, J. (2005), Foreign free riders and the high price of US medicines.

British Medical Journal, Vol 331, pp. 958-960. Retrieved 3 March 2009 from http://bmj.com/cgi/content/full/331/7522/958

Light, D.W. and Warburton, R. (2005a), Extraordinary claims require extraordinary evidence: Comment. *Journal of Health Economics* Vol 24, pp.1030-1033.

Light, D.W. and Warburton, R. (2005b), Setting the record straight in reply to Dimasi, Hansen, and Grabowski. *Journal of Health Economics* Vol 24, pp. 1045-1048.

Lillis, A. M. (1999), A framework for the analysis of interview data from multiple field research sites. *Accounting and Finance.* Vol. 39 pp. 79-105

Lincoln, Y. S. and Guba, E. G. (1985), *Naturalistic inquiry*. Newbury Park: Sage.

Lincoln, Y. S. and Guba, E. G. (2000), Paradigmatic controversies, contradictions and emergency confluences. In N. K. Denzin and Y. S. Lincoln (Eds.), *Handbook of qualitative research* (2nd ed.) Thousand Oaks: Sage (pp. 163-188).

Llewellyn, S. (2007), Case studies and differentiated realities. *Qualitative Research in Accounting & Management.* Vol. 4 No. 1, pp. 53-68

Lockhart, M., Babar, Z.U. and Garg, S. (2010), Evaluation of policies to support drug development in New Zealand, *Health Policy*, in press.

Lomas, J. (2003), Health services research, (editorial) *British Medical Journal,* Vol 327, pp. 1301- 1302.

López-Mosquera, N. and Sánchez, M. (2011), The influence of personal values in the economic-use valuation of peri-urban green spaces: An application of the means-end chain theory. *Tourism Management* Vol 32 No. 4, pp. 875–889.

Lowe, A. (2000), The construction of a network at Health Waikato: The ``towards clinical budgeting'' project. Accounting Auditing & Accountability Journal, Vol. 13 No. 1, pp. 84-114.

Luhmann, N. (1979), *Trust and Power*. New York: John Wiley and Sons

Majumdar, S.R., Chang, W. and Armstrong, P.W. (2002), Do the investigative sites that take part in a positive clinical trial translate that evidence into practice? *American Journal of Medicine,* Vol 113 No. 2, pp. 140-145.

Makadok, R. and Coff, R. (2002), The theory of value and the value of theory: Breaking new ground versus reinventing the wheel. *Academy of Management Review*, Vol 27, No. 1, pp. 10-16.

Malakoff, D. (2008), Spiraling costs threaten gridlock. *Science,* Vol 322 (October), pp. 210-213.

Mallik, A. K. and Mitra, S. (2009), Accounting and accountability: A stakeholder-agent perspective. *The IUP Journal of Accounting Research & Audit Practices*, Vol. VIII, Nos. 3 & 4, pp. 7- 20.

Marcuccio, M. and Steccolini, I., (2005), Social and Environmental Reporting in Local Authorities, *Public Management Review*. Vol.7 No.2, pp. 155–76.

Marton, F. (1981), Phenomenography - describing conceptions of the world around us. *Instructional Science*, Vol. 10, pp.177-200.

Marton, F. (1986), Phenomenography: A research approach to investigating different understandings of reality. *Journal of Thought*, Vol 21 No.3, pp. 28-43.

Marton, F. (1994), On the structure of awareness. In J. A. Bowden & E. Walsh (Eds.), *Phenomenographic research: Variations in method* (pp. 176-205). Melbourne, Australia: Office of the Director EQARD, Royal Melbourne Institute of Technology.

Mathews, M. R. (1993), *Socially Responsible Accounting,* UK, Chapman & Hall.

Mattingly, J. E. (2004). Stakeholder salience, structural development, and firm performance: Structural and performance correlates of sociopolitical stakeholder management strategies, Business & Society, Vol 43 pp. 97-114.

Mauskopf, J., Paul, J., Grant, D. and Stergachis, A. (1998), The Role of Cost-Consequence Analysis in Healthcare Decision-Making. *PharmacoEconomics,* Vol 13 No.3, pp. 277-288

McClellan, M. B; McGinnis, J. M.; Nabel, E. G. and Olsen, L. A. (2008) *Evidence-Based Medicine and the Changing Nature of Healthcare: Meeting Summary (IOM Roundtable on Evidence-Based Medicine)* available from http://www.nap.edu/catalog/12041.html

McDonagh, M.S., Miller, S. A. and Naden, E. (2000), Costs and savings of investigational drug services. *American Journal Health Systems Pharmacy*, Vol 57 No1, pp. 40-43.

McGivern, Y. (2006), *The practice of market and social research* (2nd ed.). Harlow: Pearson Education Ltd.

McGregor M. (2006), What decision-makers want and what they have been getting. *Value in Health* Vol. 9, pp. 179–180.

McGuinness, C. (2007), Participation in a clinical trial: Views of children and young people with diabetes. *Paediatric Nursing,* Vol 19 No 6, pp.37-39.

Medawar C. (1976), The social audit: a political view *Accounting, Organizations and Society* Vol 1, No 4, pp. 389-394.

Medical Expenditure Panel Survey (n.d.), Agency for healthcare research and quality. Retrieved April 14, 2009, from http://www.meps.ahrq.gov/mepsweb/

Medicines New Zealand (nd) Retrieved April 14, 2011 from http://www.medicinesnz.co.nz

Medsafe (nd) Home page Retrieved April 14, 2009, from http://www.medsafe.govt.nz/other/about.asp

Meineche-Schmidt, V., Hvenegaard, V. and Juhl, H. H. (2006), Participation in a clinical trial influences the future management of patients with gastro-oesophageal reflux disease in general practice. *Ailentary Pharmacology and Therapeutics,* Vol 24, pp.1117-1125.

Miles, P. V., Bingham, J.W. and Dilts, D. (2002), Research as a quality improvement activity. *Journal of the American Medical Association,* Vol 287 No.7, pp.843-844.

Mills, R. and Weinstein B. (2000), Beyond Shareholder Value. Reconciling the shareholder and stakeholder perspectives, *Journal of General Management*, Vol. 25, No. 3, Spring, pp. 79-93.

Milne, M. J. (1991), Accounting, environmental resource values, and non-market valuation techniques for environmental resources: A review. *Accounting, Auditing & Accountability Journal,* Vol.4 No. 3, pp.81-109.

Ministry of Health (2005), *Laboratory Claims Data Warehouse Data Dictionary Version 2.0.* Wellington: Ministry of Health.

Ministry of Health (2006), *Operational Standard for Ethics Committees: Updated edition.* Wellington: Ministry of Health.

Ministry of Health (n.d.), Structure of the New Zealand health and disability system. Accessed 24 April 2009 From http://www.moh.govt.nz/moh.nsf/indexmh/healthsystem-overview#dhbs

Mir, M.Z. and Rahaman, A. S. (2011), In pursuit of environmental excellence: A stakeholder analysis of the environmental management strategies and performance of an Australian energy company. *Accounting, Auditing & Accountability Journal* Vol. 24 No. 7, pp. 848-878.

Mitchell, R. K. and Agle, B. R. (1997), Stakeholder identification and salience: Dialogue and

Operationalization. *Proceedings of the International Association for Business and Society 1997 Destin Florida.*

Mitchell, R. K., Agle, B. R. and Wood, D. J. (1997), Toward a theory of stakeholder identification and salience: Defining the principle of who and what really counts. *Academy of Management Review* 24(4): 853-86.

Modell, S. (2005), Triangulation between case study and survey methods in management accounting research: an assessment of validity implications*, Management Accounting Research*, Vol. 16 No. 2, pp. 231-54.

Modell, S. (2009), In defence of triangulation: A critical realist approach to mixed methods research in management accounting. *Management Accounting Research* Vol 20, pp.208–221

Moffatt, S., White, M., Mackintosh J. and Howel, D. (2006), Using quantitative and qualitative data in health services research – what happens when mixed method findings conflict" [ISRCTN61522618]. *BMC Health Services Research*, Vol. 6 No. 28 doi:10.1186/1472-6963-6- 28, available from: http://www.biomedcentral.com/1472-6963/6/28

Montaner, J., O'Shaughnessy, M. and Schechter, M. (2001), Industry-sponsored clinical research: A double-edged sword. *Lancet*; Vol 358, pp. 1893–1895.

Mooney, G (2003), *Economics Medicine and Health Care (3rd Edition)*. Harlow: Pearson Education.

Mooney, G. and Lange, M. (1993), Antenatal screening: What constitutes a benefit? *Social Science and Medicine,* Vol 37*,* pp.873-878.

Moore, S. (2001), A need to try everything: Patient participation in phase I trials. *Journal of Advanced Nursing*, Vol 33 No.6, pp. 738-747.

Morgan, D. L. (1995), Why things (sometimes) go wrong in focus groups. *Qualitative Health Research,* Vol 5 No. 4, pp. 516- 523, Retrieved from http://qhr.sagepub.com

Morgan, D. L. (1988), *Focus groups as qualitative research*. Beverly Hills, CA: Sage.

Morgan, D. L. (1997), *Practical strategies for combining qualitative and quantitative methods.* Portland, OR: Portland State University Press.

Morgan, D. L. (2007), Paradigms lost and pragmatism regained: Methodological implications of combining qualitative and quantitative methods. *Journal of Mixed Methods Research*; Vol 1, pp. 48-76.

Morgan, D. L. and Scannell, A. U. (1997), *Planning focus groups*. Thousand Oaks, California: Sage Publications.

Morgan, G. and Smircich, L. (1980), The case of qualitative research, *Academy of Management Review*, Vol. 5, pp. 491-500.

Morse, J.M. (2000), Determining sample size, *Qualitative Health Research*, Vol.10 No. 1, pp. 3-5.

Morse, J. M. (2001), Using shadowed data. *Qualitative Health Research*, Vol 11, pp. 291-292.

Mueller, M. (2004), Clinical, technical, and social contingencies and the decisions of adults with HIV/aids to enroll in clinical trials. *Qualitative Health Research,* Vol 14 No 5, pp. 704-713.

Muennig P. (2007), *Cost-effectiveness analysis in health*. Jossey-Bass, San Francisco, CA.

Murphy, K. M. and Topel, R. (1998), The economic value of medical research. Accessed 12 November 2009 from http://laskerfoundation.org/advocacy/econimpact.htm

Murphy, L. and Maquire, W. (2011a), Applying mixed methods research in evaluating clinical trials, *Qualitative Research in Accounting & Management*, Vol. 8 No. 1, pp.72 - 90 trials.

Murphy, L and Maguire, W. (2011b), Quantifying the benefits and costs of conducting sponsored clinical trials in a publicly funded NewZealand hospital. Paper presented to the *Accounting and Finance Association of Australia and New Zealand (AFAANZ) Annual Conference, Darwin, 3-5 July 2011.*

Murphy, L and Maguire, W. (2011b), Quantifying the benefits and costs of conducting sponsored clinical trials in a publicly funded NewZealand hospital. Paper presented to the *Accounting and Finance Association of Australia and New Zealand (AFAANZ) Annual Conference, Darwin, 3-5 July 2011.*

National Research Council (2010), *Value in Health Care: Accounting for Cost, Quality, Safety, Outcomes, and Innovation: Workshop Summary*. Washington, DC: The National Academies Press.

Neal, B., Rodgers, A., Mackie, M. and MacMahon, S. (1996), Forty years of randomised trials in the New Zealand Medical Journal. *New Zealand Medical Journal,* Vol 109 No.1031, pp. 372-373.

Neu, D., Warsame, H. and Pedwell, K. (1998), Managing public impressions: environmental disclosures in annual reports, *Accounting, Organizations and Society*, Vol 23, No. 3 pp.

265-282.

Neu, D. and Graham, C. (2005), Editorial: Accounting research and the public interest. *Accounting, Auditing & Accountability Journal* Vol. 18 No. 5, 2005 pp. 585-591

Neumann, P. J. (2011), What Next for QALYs? *Journal of the American Medical Association*. Vol 305 No.17, pp.1806-1807.

Neville B A and Mengue B (2006). Stakeholder multiplicity: Towards an understanding of the interactions between stakeholders, *Journal of Business Ethics* Vol 66, pp. 377-391.

New Zealand Parliament (2010), *Inquiry into improving New Zealand's environment to support innovation through clinical trials*. Wellington: Committee Secretariat Health. http://www.parliament.nz/en NZ/PB/SC/MakeSub/9/2/1/49SCHE_SCF_00DBSCH_INQ_9752_1-Inquiry-into-improving-New-Zealand-s.htm

New Zealand Press Association (2008), Drug trials could be big business in New Zealand. *New Zealand Herald,* June 18 p. 10.

New Zealand Treasury (2009), Challenges and choices: New Zealand's long term fiscal statement October 2009. Persistent URL: http://www.purl.org/nzt/o-1243.

Nørreklit, H. Nørreklit, L and Mitchell, F. (2010), Towards a paradigmatic foundation for accounting practice. *Accounting, Auditing & Accountability Journal,* Vol. 23 No. 6, pp. 733-758.

Nuremburg Code (nd) accessed 2 February 2010 from http://ohsr.od.nih.gov/guidelines/nuremberg.html

Oakes, L. S., Considine, J. and Gould, S. (1994), Counting Health Care Costs in the United States: A Hermeneutical Study of Cost Benefit Research, *Accounting, Auditing & Accountability Journal*, Vol. 7 No 3, pp.18 - 49

Obeng, E. (2008), Bankable strategies. *Accountancy Age,* Feb 7 p1.

O'Cathain, A., Murphy, E. and Nicholl, J. (2007), Integration and publications as indicators of "yield" from mixed methods studies. *Journal of Mixed Methods Research,* Vol 1 No. 2, pp. 147–163.

O'Connell, D. and Mosconi, P. (2006), An active role for patients in clinical research? *Drug Development Research* Vol 67, pp.188–192.

O'Dwyer, B. (2005), The construction of a social account: A case study in an overseas aid

Agency. *Accounting, Organizations and Society* Vol 30, pp. 279–296

Ono, S. and Kodama, Y. (2000), Clinical trials and the new good clinical practice guidelines in Japan. *PharmacoEconomics,* Vol 18 No.2, pp. 125-141.

Owen, D. L., Swift, T. A. and Hunt, K. (2001), Questioning the role of stakeholder engagement in social and ethical accounting, auditing and reporting. *Accounting Forum*, Vol 25 No.3, pp. 264–282.

Owen, D. L., Swift, T. A., Humphrey, C., and Bowerman, M. (2000). The new social audits: accountability, managerial capture or the agenda of social champions? *European Accounting Review*, Vol 9, No.1, pp. 81–98.

Pack, S. J. (2010), *Aristotle, Adam Smith and Karl Marx: on some fundamental issues in 21st century political economy*. Massachusetts: Edward Elgar Publishing Co.

Panel on Return on investment in Health Research, (2009a), *Making an impact: A preferred framework and indicators to measure return on investment in health research.* Canadian Academy of Health Sciences, Ottawa, ON, Canada. *Accessed 15 February 2010 from* http://www.cahs-acss.ca/e/assessments/completedprojects.php

Panel on Return on investment in Health Research, (2009b), *Appendices - Making an impact: A preferred framework and indicators to measure return on investment in health research.* Canadian Academy of Health Sciences, Ottawa, ON, Canada.
Accessed 15 Feb 2010
from http://www.cahs-acss.ca/e/assessments/completedprojects.php

Pardes, H., Manton, K.G., Lander, E.S., Tolley, H.D., Ullian, A.D. and Palmer, H. (1999), Effects of medical research on health care and the economy. *Science* Vol 283, pp36-37.

Parker, L. D. (2005), Social and environmental accountability research: A view from the commentary box. *Accounting, Auditing & Accountability Journal* Vol 18 No. 6, pp. 842-860.

Patton, M. Q. (1990), *Qualitative evaluation and research methods* (2nd ed.). Newbury Park, CA: Sage.

Paz, D.A. (2005), Economic behavior and informed consent. *Journal of the American Medical Association,* Vol 293 No.17, pp. 2092.

Perrín, R. S. and López, F. J. (2008), Incremental Drug Treatment Cost in HIV-Positive Patients

in Industry-Sponsored Clinical Trials. *The Annals of Pharmacotherapy*: Vol. 42, No. 11, pp. 1586-1591.

PHARMAC (2005), *Recommended methods to derive clinical inputs for proposals to PHARMAC Version 1B*, 20 July.

PHARMAC (2006), *PHARMAC operating policies and procedures, 3rd edition* - January 2006

PHARMAC (2007), *Prescription for pharmacoeconomic analysis: Methods for cost-utility analysis.* Final May Accessed 15 Feb 2010 from http://www.pharmac.govt.nz/2007/06/19/PFPAFinal.pdf

PHARMAC. (n.d.), *History*. Retrieved June 1, 2008, from www.pharmac.govt.nz/healthpros/AboutPHARMAC/history

Phillips, R. A. (1997), Stakeholder theory and a principle of fairness. *Business Ethics Quarterly* Vol 7 No.1 pp. 51-66.

Pizzini, M. J. (2006), The relation between cost-system design, managers evaluations of the relevance and usefulness of cost data, and financial performance: an empirical study of US hospitals. *Accounting, Organizations and Society* Vol. 31 pp. 179–210

Porter, M.E. (2008), Defining and introducing value in health care. In McClellan, M. B; McGinnis, J. M.; Nabel, E. G. and Olsen, L. A. [Ed} *Evidence-Based Medicine and the Changing Nature of Healthcare: Meeting Summary (IOM Roundtable on Evidence-Based Medicine)* available from http://www.nap.edu/catalog/12041.html

Porter, M.E. (2010), What is value in health care? *New England Journal of Medicine.* Vol 363 pp. 2477-2481 (10.1056/NEJMp1011024).

Post, J. E., Preston, L. E. and Sachs, S. (2002), *Redefining the corporation: Stakeholder management and organizational wealth*. Stanford: Stanford University Press.

Preston, A.M. (1992), The birth of clinical accounting: A study of the emergence and transformation of discourses on costs and practices of accounting in US hospitals, *Accounting, Organizations and Society*, Vol. 17 No. 1, pp. 63-100.

Quintiles (2011), *The New Health Report: Exploring Perceptions of Value and Collaborative Relationships Among Biopharmaceutical Stakeholders* Accessed 6/4/2012 from http://www.quintiles.com/newhealthreport/

Quirk, J., Schrag, D., Radzyne, R. M., Rubin, D., Nelson, P. J. and Bosl, G.J. (2000), Clinical trial costs are similar to and may be less than standard care and inpatient (INPT) charges

at an academic medical center (AMC) are similar to major, minor, and non-teaching hospitals. *Proceedings of the Annual Meeting of the American Society of Clinical Oncology 1695.*Accessed 17 Sept 2008 from http://www.oncolink.org/conferences/article.cfm?c=3&s=6&ss=20&id=256

Ramsey, S. D. (2008)**,** How should we value lives lost to cancer? *Journal of the National Cancer Institute,* Vol 100 No.24, pp. 1742-1743.

Rappaport, A. (1986), *Creating Shareholder Value*. New York, The Free Press.

Rea, D. M. (1994), Better informed judgements: Resource management in the NHS. *Accounting, Auditing & Accountability Journal,* Vol 7 No.1, pp. 86-110.

Reichert, J.M. and Milne C. P. (2002), Public and private sector contributions to the discovery and development of 'impact' drugs. *American Journal of Therapeutics;* Vol 9 No. 12 pp. 543-555 {previously published as *a Tufts Center for the Study of Drug Development white paper.* Boston MA: The Center, May, 2002} *Accessed 15 Feb 2010 from* http://csdd.tufts.edu./_documents/www/Doc_233_7207_826.pdf

Researched Medicines Industry Association of New Zealand (2006), *Researched Medicines Industry Association of New Zealand Incorporated Code of Practice***.** Retrieved 12 August, 2008, from http://www.rmianz.co.nz

Reynolds, T. J. and Gutman, J. (1988). Laddering theory, method, analysis, and interpretation. *Journal of Advertising Research*, Vol 28, pp.11-31.

Rice, P. and Ezzy, D. (2000), *Qualitative Research Methods – A Health Focus*. Melbourne: Oxford University Press.

Richardson, L. (2000), New writing practices in qualitative research. *Sociology of Sport Journal,* Vol 17, pp. 5-20.

Richardson, R., Shaw, I. and Nolan, S., (2003), A perspective on New Zealand's medicines and regulatory environment. *International Journal of Pharmaceutical Medicine*, Vol 17, No. 1, pp. 17-22.

Ridley, D. B., Grabowski, H. G. and Moe, J. L. (2006), Developing drugs for developing Countries, *Health Affairs;* Vol 25 No 2, pp. 313-324.

Roberts, R. W. and Mahoney, L. (2004), Stakeholder conceptions of the corporation: Their meaning and influence in accounting research. *Business Ethics Quarterly*, Vol. 14, No. 3, pp. 399-431.

Robinson, J.M. and Trochim, W. M. (2007), An examination of community members', researchers' and health professionals' perceptions of barriers to minority participation in medical research: an application of concept mapping. *Ethnicity and Health* Vol 12, No. 5, pp. 521-539.

Robson, N. (2007), Costing, funding and budgetary control in UK hospitals: An historical reflection. *Cardiff Working Papers in Accounting and Finance.* Cardiff: Cardiff University.

Roche, K.; Paul, N.; Smuck, B.; Whitehead, M.; Zee, B.; Pater, J.; Hiatt, M. and Walker, H. (2002), Factors Affecting Workload of Cancer Clinical Trials: Results of a Multicenter Study of the National Cancer Institute of Canada Clinical Trials Group. *Journal of Clinical Oncology,* Vol 20 No. 2 pp.545-556.

Romney, A., Batchelda, W. and Weller, S. (1986), Culture as consensus: A theory of culture and informant accuracy. *American Anthropologist,* Vol 88, pp. 313-338.

Ronte, H. (1998), Value based management. *Financial Management,* Vol 76, No 1, pp.38-38.

Rosen, S. (1988), The value of changes in life expectancy, *Journal of Risk and Uncertainty*, Vol. 1 No.3 pp. 285-304.

Ross, L. E., Stroud, L. A., Rose, S. W. and Jorgensen, C. M. (2006), Using telephone focus groups methodology to examine the prostate cancer screening practices of African-American primary care physicians. *Journal of the National Medical Association,* Vol 9 No.8, pp. 1296 - 1302.

Rosser R. and Kind P. (1978), A scale of valuations of states of illness: Is there a social consensus? *International Journal of Epidemiology*; Vol 7, pp.347-58.

Rowley, T. J. (1997), Moving beyond dyadic ties: A network theory of stakeholder influences, *The Academy of Management Review* Vol. 22 No. 4, pp. 887-910.

Ryan, S. (2009), Benefits of conducting commercial clinical trials in a NZ public hospital. Paper presented at the New Zealand Clinical Research Conference Auckland 20-21 August

Sade, R. M. (2009)**,** Dangerous liaisons? Industry relations with health professionals. *Journal of Law and Medical Ethics,* Vol 37, pp.398–400.

Sage, M. and Jellie A. (2003), *The thin edge of the wedge: Balancing budgets in biotechnology*. Simpson Grierson X-Tech Group (Feb).

Sale, J.E.M. (2007), What do primary care nurses and radiation therapists in a Canadian cancer

centre think about clinical trials? *Journal of Evaluation in Clinical Practice,* Vol 13 No. 2 pp. 186-191.

Sale, J.E.M., Lohfeld, L.H. and Brazil, K. (2002), Revisiting the quantitative-qualitative debate: Implications for mixed-methods research. *Quality and Quantity,* Vol 36, pp. 43–53

Salterio, S. (1994), Researching for accounting precedents: Learning, efficiency, and effectiveness. *Contemporary Accounting Research*, Vol 11, No. 1, pp. 515 - 542

Samuel, S., Dirsmith, M. W. and McElroy, B. (2005), Monetized medicine: from the physical to the fiscal. *Accounting, Organizations and Society* Vol. 30, pp. 249–278.

Samuelson, P. and Nordhaus, W. (2001), *Economics (17th edition)* New York :McGraw-Hill Higher Education.

Sandelowski, M. (2000), Whatever happened to qualitative description? *Research Nursing and Health,* Vol. 23, pp. 334-340.

Saunders, M., Lewis, P. and Thornhill, A. (2007), *Research Methods for Business Students, 4th edn.* Harlow, UK: Prentice Hall.

Scapens, R. W. (1991), *Management Accounting: A Review of Contemporary Developments*, Macmillan World Publishing Corp., London.

Scharke, C. C. (2008), Measuring trust in clinical research. *Monitor* September pp.12-14.

Scheifele, D. W. (1997), Clinical trials and tribulations: A personal view of interacting with pharmaceutical manufacturers. *Clinical and Investigative Medicine*, Vol 20 No.3, pp. 188-192.

Schmitt, C.M. (2006), Research in clinical practice. *Gastrointestinal Endoscopy Clinics of North America,* Vol 16 No. 4, pp. 751-73.

Securities Commission, New Zealand (nd) accessed 24/4 2011 from http://www.seccom.govt.nz/publications/documents/governance-principles/05.shtml)

Sen, A. (1979), Personal utilities and public judgements: Or what's wrong with welfare economics? *The Economic Journal*, Vol 89, pp.537–558.

Sen, A. (1982), *Choice, welfare and measurement*. Cambridge, MA: Harvard University Press.

Sen, A. (2000), The discipline of cost-benefit analysis. *Journal of Legal Studies* Vol 29 No.2, pp. 931-952

Sequin, D.A. (1990), My role as a research nurse coordinator. *Critical Care Nursing* Vol 12, pp. 39-44

Shiel A, Di Ruggiero E. (2009), Assessing the return on Canada's public investment in population and public health research: methods and metrics. In: *Return on investments in health research*. Ottawa (ON): Canadian Academy of Health Sciences; 2009. p. A42–74. Accessed Jan 21 2010, www.cahs-acss.ca/e/assessments/completedprojects.php

Shields, M.D. (1997), Research in management accounting by North Americans in the 1990s. *Journal of Management Accounting Research*, Vol. 9, pp. 3-61.

Shiozawa, Y. (1999), Economics and accounting: A comparison between philosophical backgrounds of the two disciplines in view of complexity theory. *Accounting Auditing & Accountability Journal*, Vol. 12, pp. 19-38

Scholl, H. J. (2001). Applying stakeholder theory to e-government: Benefits and limits. *Proceedings of the 1st IFIP Conference on E-Commerce, E-Business, and E-Government (I3E 2001, October 3-5)*, Zurich, Switzerland

Schuber, P. (2008), Measuring attitudes toward participation in cancer treatment and cancer prevention trials: The attitude toward cancer trial scales (ACTS). *Journal of Nursing Measurement,* Vol 16, pp. 138-152.

Schwandt, T. A. (2001), *Dictionary of qualitative inquiry (2nd ed.).* Thousand Oaks, CA: Sage.

Silversides, A. (2009), Clinical trials: the muddled Canadian landscape. *Canadian Medical Association Journal,* Vol 180 No.1, pp. 20-22.

Simone, J.V. and Lyons J. (1998), The evolution of cancer care for children and adults. *Journal of Clinical Oncology*. Vol 16, pp. 2904-2905.

Sinden, A., (2004), Cass Sunstein's cost–benefit lite: economics for liberals. *Columbia Journal of Environmental Law* Vol 29, pp.191–241.

Smith G. E. and Huntsman C. A. (1997), Reframing the metaphor of the citizen-government relationship: A value-centered perspective. *Public Administration Review*, Vol. 57, No. 4, pp. 309-318 URL: http://www.jstor.org/stable/977312

Smith, G.P. (2008), *Distributive justice and the new medicine.* Cheltenham: Edward Elgar Publishing Limited

Smith, J.K. (1983), Quantitative v qualitative research: An attempt to classify the issue. *Educational Researcher,* Vol 12, pp. 6-13.

Smith, J. K. and Heshusius, L. (1986), Closing down the conversation: The end of the quantitative– qualitative debate among educational inquirers. *Educational Researcher,*

Vol 15, pp. 4–13.

Sørensen, A. (2002), Value, business and globalisation: Sketching a critical conceptual framework. *Journal of Business Ethics*, Vol. 39, No. 1/2, Four Teenth Annual Conference of the European Business Ethics Network (EBEN), pp. 161-167.

Sørensen, J. E. and Grove, H. D. (1977), Cost-outcome and cost-effectiveness analysis: Emerging nonprofit performance evaluation techniques. *The Accounting Review*, Vol. 52, No. 3, pp. 658-675.

Spash, C. L. (2007), The economics of climate change impacts à la Stern: Novel and nuanced or rhetorically restricted? *Ecological Economics* Vol 63 No.4, pp. 706-713.

Starks, S.H. and Brown Trinidad, S. (2007). Choose Your Method: A Comparison of Phenomenology, Discourse Analysis, and Grounded Theory. *Qualitative Health Research,* Vol 17, pp. 1372-1380.

Svendsen, A. (1998), *The Stakeholder Strategy: Profiting from Collaborative Business Relationships*, Berrett-Kohehler Publishers, San Francisco, CA.

Tashakkori, A. and Creswell, J. W. (2007), The new era of mixed methods", *Journal of Mixed Methods Research,* Vol.1, pp. 3-7.

Tashakkori A and Teddlie C (Eds.) (2003), *Handbook of mixed methods in social and behavioural research.* Thousand Oaks, CA: Sage.

Tay, J. and Tinmouth, A. (2007), Observational studies: What is a cohort study? *Transfusion,* Vol 47*,* July pp. 1115-1117.

Taylor, K. M. and Kelner, M. (1987), Informed consent: The physicians' perspective. *Social Science and Medicine,* Vol 24 No2, pp. 135-143.

Taylor, M. (1996), When rationality fails, in J. Friedman (ed.), *The Rational Choice Controversy.* New Haven CT: Yale University Press, pp. 223–35.

Teddlie, C. and Tashakkori, A. (2009), *Foundations of mixed methods research: Integrating quantitative and qualitative approaches in the social and behavioral sciences*. Thousand Oaks, CA: Sage.

The International Federation of Accountants (2010) Exposure Draft of IFAC Policy Position Paper #4, *A Public Interest Framework for the Accountancy Profession*, Accessed 19/4/2012 from http://www.ifac.org.

The New Zealand Herald, (2008, Friday, August 16). The insider: What's going on behind the

scenes. *The Business Herald,* p. 23.

The New Zealand Parliament Health Select Committee (2011), *Inquiry into improving New Zealand's environment to support innovation through clinical trials. Report of the Health Committee.* Accessed 8 June 2011 from: http://www.parliament.nz/NR/rdonlyres/5AFC2393-05CF-44DB-8BF1-DD501A057408/193163/DBSCH_SCR_5154_InquiryintoimprovingNewZealandsenvi.pdf

The Nuremberg Code (1953) [from *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10.* Nuremberg, October 1946–April 1949. Washington, D.C.: U.S. G.P.O, 1949–1953.] Accessed 21 August 2009 from http://www.ushmm.org/research/doctors/Nuremberg_Code.htm

Thomson, I., and Bebbington, J. (2004), Social and environmental reporting in the UK: a pedagogic evaluation. *Critical Perspectives on Accounting*, Vol 16, pp. 507–533

Tilling, M. V. (2004), Some thoughts on legitimacy theory in social and environmental accounting *Social and Environmental Accountability Journal*. Vol. 24, No. 2, pp.3-7

Tinker, A. M. (1980), Towards a political economy of accounting: An empirical illustration of the Cambridge controversies. *Accounting, Organizations and Society*. Vol 5, No. 1, pp. 147-160.

Toms, S. (2010), Value, profit and risk: accounting and the resource-based view of the firm *Accounting, Auditing & Accountability Journal* Vol. 23 No. 5, pp. 647-670.

Torralba, K.D., Quismorio, F.P. and Khan, N.A. (2009), Clinical trials and public trust: The geographical shift to the Asia-Pacific region. *International Journal of Rheumatic Diseases* Vol 12, pp. 186-191.

Town, C. (1998), Project control and earned value management. *Management Accounting (UK)* Vol 76 No.8, pp.22–24.

Twinn, S. (2003), Status of mixed methods research in nursing. In: Tashakkori, A, Teddlie, C (eds), *Handbook of Mixed Methods in Social and Behavioral Research.* Thousand Oaks, CA: Sage. pp. 541–556.

Ullmann, A.E. (1985), Data in search of a theory: a critical examination of the relationships among social performance, social disclosure and economic performance of US firms, *Academy of Management Review,* Vol. 10 No. 3, pp. 540-57.

United States General Accounting Office (1999), *NIH clinical trials: Various factors affect patient participation.* Report to Congressional Requesters Health Education and General Services Division: Washington. Accessed 21 August 2009 from www.gao.gov/archive/1999/he99182.pdf

Van Peursem, K. A., Pratt, M. A. and Lawrence, S. R. (1995), Health management performance: A review of measures and indicators. *Accounting, Auditing & Accountability Journal*, Vol. 8 No. 5, pp. 34-70.

Viscusi, W. K. and Aldy, J. E. (2003), The value of a statistical life: A critical review of market estimates throughout the world, *Journal of Risk and Uncertainty* Vol 27 No3, pp. 239-256.

Wallace, L. (2004), Freedom as progress Laura Wallace interviews Nobel Prize–winner Amartya Sen. *Finance & Development* September, pp. 4-7

Watson, E. (2006), *Pharmaceutical research and development in New Zealand - on the brink of abyss*: Auckland: Nazadel Ltd.

Webb, S. and Kevern, J. (2001), Focus groups as a research method: a critique of some aspects of their use in nursing research. *Journal of Advanced Nursing,* Vol 33. pp. 798–805.

Weinstein, M. C. and Stason, W. B. (1977), Foundations of cost-effectiveness analysis for health and medical practices. *New England Journal of Medicine*, Vol 296 No 13, pp.716–721.

Wheeler, D., Colbert, B. and Freeman, R.E. (2003), Focusing on value: reconciling corporate social responsibility, sustainability and a stakeholder approach in a network world, *Journal of General Management*, Vol. 28 No. 3, pp. 1-28.

White, C. D. (2004), Randomised controlled trials of palliative care – A survey of the views of advanced cancer patients and their relatives. *European Journal of Cancer,* Vol 44 No.13, pp. 120-129.

Whiting, L. (2008), Semi-structured interviews: guidance for novice researchers. *Nursing Standard;* Feb 13, pp. 22 – 23.

Whittington, D and MacRae, D (1986), The Issue of Standing in Cost-Benefit Analysis. *Journal of Policy Analysis and Management*, Vol. 5, No. 4, pp. 665-682.

Williams, A. (1972), Cost benefit analysis: Bastard science or insidious poison in the body politic. *Journal of Public Economics,* Vol 1, pp. 199 -216.

Williams, A. (1988), Priority setting in private and public health care: A guide through the

ideological jungle. *Journal of Health Economics* Vol 7 No 2, pp. 173-183.

Williams, C.J., Shuster Jr. J.L., Clay, O.J. and Burgio, K.L. (2006), Interest in research participation among hospice patients, caregivers, and ambulatory senior citizens: Practical barriers or ethical constraints. *Journal of Palliative Medicine,* Vol 9 No 4, pp. 968-974.

Williams, S.J., Gabe, J. and Davis, P. (2008), The sociology of pharmaceuticals progress and prospects**.** *Sociology of Health & Illness,* Vol 30 No 6, pp.813-824.

Winfrey, J. C. (1993), Derailing value theory: Adam Smith and the Aristotelian tradition. Journal of the History of Economic Thought, 15, pp. 301-319.

Woolf, S. and Johnson, R. (2005), The break-even point: When medical advances are less important than improving the fidelity with which they are delivered. *Annals of Family Medicine,* Vol 3 No.6, pp. 545-552.

World Health Organisation (2008), Core health indicators: Country, indicator and year selection. Accessed 9/3/2012 from http://apps.who.int/whosis/database/core/core_select.cfm

World Medical Association (nd) WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. Accessed 9/3/2012 from http://www.wma.net/en/30publications/10policies/b3/index.html

Worth, R., Home, P., Johnston, D., Anderson, J., Ashworth, L., Burrin, J. M., Appleton, D., Binder, C. and Alberti, K. G. (1982), Intensive attention improves glycaemic control in insulin-dependent diabetes without further advantage from home blood glucose monitoring: Results of a controlled trial. *British Medical Journal*. Vol*285* No.6350, pp.1233-1240.

Wright, J.R. and Levine, M.N. (2003), Researching the cost of research. *Journal of Clinical Oncology*, Vol 21 No.22 pp. 4081-4082

Wright, J.R., Roche, K., Smuck, B., Cormier, J., Cecchetto, S., Akow, M., Pilatzke, S. & Pritchard, K. (2005), Estimating per patient funding for cancer clinical trials: An Ontario based survey. *Contemporary Clinical Trials,* Vol 26 No. 4, pp. 421-429.

Wynia, M. and Boren D. (2009), Better regulation of industry-sponsored clinical trials is long overdue. *Journal of Law and Medical Ethics,* Vol 37, pp. 410–419.

Wynn-Williams, K. (2011), Organisational effectiveness: debates behind measurement issues in

the public health sector. Working paper Permanent link: http://hdl.handle.net/10523/1589

Yin, R. K. (2003), *Case study research: Design and methods* (3rd edition). Newbury Park: Sage.

Young, S. and Feigin, B. (1975), Using the Benefit Chain for Improved Strategy Formulation *Journal of Marketing*, July, pp. 72-74.

Zajac, E. (1995), *Political Economy of Fairness.* Cambridge, Mass.: The MIT Press.

Ziller, A. and Phibbs, P. (2003), Integrating social impacts into cost benefit analysis: A participative method: case study: the NSW Area Assistance Scheme, *Impact Assessment and Project Appraisal,* Vol 21 Nov 2, pp. 141-162.

Zycher, B., DiMasi, J.A. and Milne, C-P. (2008), *The truth about drug innovation: thirty-five summary case histories on private sector contributions to pharmaceutical science*. Manhattan Institute Center for Medical Progress (6, June) Accessed 20 March 2009, http://www.manhattan-institute.org/html/mpr_06.htm

APPENDICES

Appendix 1: Interview Information Sheet

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School of Accounting & Corporate Governance

INTERVIEW INFORMATION SHEET

A cost benefit analysis of conducting sponsored clinical drug trials in a publicly funded New Zealand hospital.

INTRODUCTION

You are invited to take part in an interview conducted by Lyn Murphy on _____date at _____time_____. Your participation in this study is entirely voluntary, and if you wish to withdraw from the study or to leave, you may do so at any time, and you do not need to give any reasons or explanations for doing so. If you do withdraw from the study, this will have no effect on your relationship with Counties Manukau District Health Board.

This is a New Zealand-based PhD project which is being supervised by the University of Tasmania.

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ABOUT THE STUDY

What are the aims of the study?
The purpose of this study is to find out about clinical drug trials; we will discuss our general ideas about the benefits and costs of clinical drug trials
How were participants selected for this study, and who selected them?

Participants have been selected by the researchers to represent the following groups
Politicians
Pharmaceutical companies
Counties Manukau District Health Board Staff
Clinical Researchers
Participants in clinical drug trials

Care givers and support people of those involved in clinical drug trials

How many participants will be involved?
We will be selecting approximately 30 people to be interviewed. In addition we intend running five focus groups each involving 6-8 people and selecting others to answer survey questions.

Where will the study be held?
We will be meeting on _____date at _____time _____.

What is the time span for the study?
The session will begin at _____ and end at _____.

What will happen during the study?
You will be asked a number of questions about the costs and benefits of clinical drug trials. I know that people have a great many different ideas on clinical drug trials, and I am very interested in hearing your thoughts on this subject. I will be recording the interview. I will keep that tape and anything you say completely confidential. My first priority is to protect your privacy. The tapes will be transcribed and the transcription tapes will be securely stored for 10 years after which time they will be destroyed. You will be required to attend one interview which will take no more than thirty minutes.

BENEFITS RISKS AND SAFETY

What are the benefits of the study?
This study will assist us to better understand the costs and benefits of clinical drug trials.

What are the risks and/or inconveniences of the study?
In an interview people may reveal information that they regard as private and confidential. To prevent violations to your own or others' privacy, you are asked not to talk about any of your own or others' private experiences that you would consider too personal or revealing. This is a non-therapeutic study.

PARTICIPATION

Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part this will not affect any future care or treatment. If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason and this will in no way affect your continuing health care**.**

GENERAL

Where can you get more information about the study?
Contact the researchers whose names and details are provided on the first page of this information sheet.

You may have a friend, family or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require. You do not have to answer all the questions, and you may leave the focus group at any time.

CONFIDENTIALITY

No material which could personally identify you will be used in any reports on this study. I will be recording the interview session. I will keep that tape and anything you say completely confidential. The tapes will be transcribed and the transcription records will be securely stored at Manukau Institute of Technology for 10 years after which time they will be destroyed.

RESULTS

The interviews form part of a large PhD project. The transcription from your interview will be sent to you for your verification shortly after the interviews have been completed.
STATEMENTS OF ETHICAL APPROVAL
This study has received ethical approval from the Northern Y Regional Ethics Committee, ethics reference number NTY/09/04/037

If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.
Telephone: (NZ wide) 0800 555 050
Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
Email (NZ wide): advocacy@hdc.org.nz

This study has also been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au <mailto:human.ethics@utas.edu.au>. The Executive Officer is the person nominated to receive complaints from research participants. Please quote the ethics reference number H10522

Appendix 2: Statement of Informed Consent.

Private Bag 86 Hobart
Tasmania 7001 Australia
Phone (03) 6226 2266 Fax (03) 6226 7845

School of Accounting & Corporate Governance

UTAS

STATEMENT OF INTERVIEW INFORMED CONSENT

I,_____ agree to participate in this research project on 'the costs and benefits of conducting commercially sponsored clinical drug trials' that is being conducted by Lyn Murphy, a PhD student of the University of Tasmania

I understand that this is a New Zealand-based PhD study which is supervised by the University of Tasmania.

I understand that the purpose of this study is to hold an interview to find out about clinical drug trials. I will be asked to discuss my general ideas about the benefits and costs of clinical drug trials.

I understand the study involves an interview that approximately twenty minutes or less, which may be audio taped.

I understand that my participation in this study is entirely voluntary, and that if I wish to withdraw from the study or to leave, I may do so at any time, and that I do not need to give any reasons or explanations for doing so. If I do withdraw from the study, I understand that this will have no effect on my relationship with Counties Manukau District Health Board or any other organisation or agency.

I understand that to prevent violations to my own or others' privacy, I have been asked not to talk about any of my own or others' private experiences that I would consider too personal or revealing.

I understand that all the information I give and the names of all the people in the study will be kept confidential.

I understand that I may not receive any direct benefit from participating in this study, but my participation may help others in the future.

The members of the research team have offered to answer any questions I may have about the study and what I am expected to do.

I have read and understand this information and I agree to take part in the study.

_____ _____

Today's Date Your Signature

If you have any concerns about this study please contact one of the following:

Investigator:

Lyn Murphy, Manukau Institute of Technology, Bairds Rd, Otara, Manukau City Phone: 968 8000. Email lyn.murphy@manukau.ac.nz

Supervisor:

Dr William Maguire**,** Senior lecturer School of Accounting and Corporate Governance**,** University of Tasmania**,** Private Bag 86**,** Hobart**,** Tasmania 7001**,** Australia**.** Email: william.maguire@utas.edu.au

Co supervisor:

Dr Willem Fourie, Deputy Head of the Department of Nursing and Health Studies, Research Development Leader Manukau Institute of Technology Otara Rd Otara. Manukau City Phone: Work: 968 8606 Mobile: 027 5688606 Email willem.fourie@manukau.ac.nz
STATEMENTS OF ETHICAL APPROVAL
This study has received ethical approval from the Northern Y Regional Ethics Committee, ethics reference number NTY/09/04/037

If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.
Telephone: (NZ wide) 0800 555 050
Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
Email (NZ wide): advocacy@hdc.org.nz

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APPENDIX 3: FOCUS GROUP INFORMATION SHEET.

Private Bag 86 Hobart
Tasmania 7001 Australia
Phone (03) 6226 2266 Fax (03) 6226 7845

School & Corporate

FOCUS GROUP INFORMATION SHEET

A cost benefit analysis of conducting sponsored clinical drug trials in a publicly funded New Zealand hospital.

INTRODUCTION

You are invited to take part in a focus group that we holding on _____date at _____time at the Manukau Institute of Technology. Your participation in this study is entirely voluntary, and if you wish to withdraw from the study or to leave, you may do so at any time, and you do not need to give any reasons or explanations for doing so. If you do withdraw from the study, this will have no effect on your relationship with Counties Manukau District Health Board.

This is a New Zealand research project which is being supervised by the University of Tasmania.

CONTACTS

Investigator:

Lyn Murphy, Manukau Institute of Technology, Bairds Rd, Otara, Manukau City Phone: 968 8000. Email lyn.murphy@manukau.ac.nz

Supervisor:

Dr William Maguire**,** Senior lecturer School of Accounting and Corporate Governance**,** University of Tasmania**,** Private Bag 86**,** Hobart**,** Tasmania 7001**,** Australia**.** Email: william.maguire@utas.edu.au

Co supervisor:

Dr Willem Fourie, Deputy Head of the Department of Nursing and Health Studies, Research Development Leader Manukau Institute of Technology Otara Rd Otara. Manukau City Phone: Work: 968 8606 Mobile: 027 5688606 Email willem.fourie@manukau.ac.nz

ABOUT THE STUDY

What are the aims of the study?

The purpose of this study is to hold a group interview to find out about clinical drug trials; we will discuss our general ideas about the benefits and costs of clinical drug trials

How were participants selected for this study, and who selected them?

Participants were selected by the researchers from those recently involved in a clinical drug trial which took place at Middlemore Hospital.

How many participants will be involved?

We intend running five focus groups each involving 6-8 people. In addition we will be selecting some people to be interviewed and others to answer survey questions.

Where will the study be held?

We will be meeting on _____date at _____time at the Manukau Institute of Technology North Campus. Enclosed with this letter is a map and directions which show you how to get to the

Manukau Institute of Technology. There is free parking available on site. We will be meeting in room _____ and the staff at the front desk will be happy to show you where that room is.

What is the time span for the study?
The session will begin at _____ and end at _____. A light lunch will be provided at the start of the focus group. We know how valuable your time is, and we will respect everyone's schedules by both starting and ending on time.

What will happen during the study?
You will be part of a group of about six to eight people mainly from the local area who have had some involvement in clinical drug trials. We know that people have a great many different ideas on clinical drug trials, and we are very interested in hearing your thoughts on this subject. Most of the time you are there you will be talking among yourselves in a group discussion. We will be recording that session so that we have a good sense of what people said. We will keep that tape and anything you say completely confidential. We don't expect anyone to be saying anything too threatening, but even so, our first priority is to protect your privacy. The tapes will be transcribed and the transcription tapes will be securely stored for 10 years after which time they will be destroyed. You will be required to attend one focus group which will take no more than 2 hours.

BENEFITS RISKS AND SAFETY

What are the benefits of the study?
This study will assist us to better understand the costs and benefits of clinical drug trials.

What are the risks and/or inconveniences of the study?
In a focus group people may reveal information that they regard as private and confidential. To prevent violations to your own or others' privacy, you are asked not to talk about any of your own or others' private experiences that you would consider too personal or revealing. This is a non-therapeutic study

Will participants be reimbursed for their expenses?
Expenses as a result of participation in the project will be reimbursed.

PARTICIPATION

Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part this will not affect any future care or treatment. If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason and this will in no way affect your continuing health care**.**

GENERAL

Where can you get more information about the study?
Contact the researchers whose names and details are provided at the end of this information sheet.
You may have a friend, family or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require. You do not have to answer all the questions, and you may leave the focus group at any time.

CONFIDENTIALITY

No material which could personally identify you will be used in any reports on this study. We will be recording the focus group session. We will keep that tape and anything you say completely confidential. The tapes will be transcribed and the transcription records will be securely stored at Manukau Institute of Technology for 10 years after which time they will be destroyed.

RESULTS

The focus groups form part of a large PhD project. The results of the focus groups will be sent to you for your verification shortly after the groups have been completed.

STATEMENTS OF ETHICAL APPROVAL

This study has received ethical approval from the Northern Y Regional Ethics Committee, ethics reference number NTY/09/04/037
If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.
Telephone: (NZ wide) 0800 555 050
Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
Email (NZ wide): advocacy@hdc.org.nz
This study has also been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. Please quote the ethics reference number H10522

APPENDIX 4: INITIAL TELEPHONE SCRIPT – FOCUS GROUPS.

(some minor adjustments will be made depending on the participant group eg staff, caregiver etc which the potential participant is part of)
Contacting the potential participant.
Hello may I please speak to _____(name)?
If the person is not at home:
When would be a good time to reach him or her?
If the person has moved try to get a new phone number.
Explaining the project.
My name is Lyn Murphy and I am calling from Manukau Institute of Technology
You were recently involved in a clinical drug trial which took place at Middlemore Hospital. Now we are holding a focus group to follow up on that project, and I want to offer you a chance to be part of that. This is a focus group that will last 2 hours and all expenses as a result of participation in the project will be reimbursed.
You would get together with other people involved with clinical drug trials to have a discussion and answer some questions for us. There would just be one meeting.
Can I tell you a little more about this?
First of all the session that we are trying to set up on (day) at_____. Is that something that could fit into your schedule?
If participant is not available, offer times for other focus groups. If not available at all thank the person and end call.
If the participant is available, continue with:
We want to find out more about the benefits and costs of clinical drug trials. Right now we are trying to put together a group of people involved with clinical drug trials so we can hear your thoughts.
We are especially interested in finding out from (name of participant group) think about clinical drug trials. This might influence the way trials are conducted in the future.
But all that is in the future. Right now this focus group will require a once only commitment of 2 hours.
We won't try to sell you anything and we won't try to sign you up for anything else. Does this sound like it would work for you?
Scheduling the session
The session would be at Manukau Institute of Technology and, again it will be on_____
We would start with refreshments at_____and then begin the session at _____We will end at _____ If I do put your name down it is very important that we have everyone show up. Do you think you can come?
It's also very important that you be there by_____. Will you have any problems getting there on time?
Again expenses as a result of participation in the project will be reimbursed.The group itself will consist of six to eight other people, all who, like yourself, have had some involvement in clinical drug trials.
Most of the time you are there you will be talking among yourselves in a group discussion.
You are welcome to bring any family or caregivers you want with you. Do you have anyone you would like to bring along?
We will be recording that session so that we have a good sense of what people said. We will keep that tape and anything you say completely confidential. We don't expect anyone to be saying anything too threatening, but even so, our first priority is to protect your privacy.
Also, I want to emphasise that once you come to this session, everything you do there will be completely voluntary, and you will be free to leave at any time for any reason.
I'd like to mail you a letter confirming your participation in this focus group, along with a map and a reminder of the date and time. What is the best address to send that to? (get mailing address)

I also need to remind you that we will be starting right on time at _____ on _____
So, it is very important that you try to get there on time.
So everyone remembers, we will be calling you back the day before the group to remind you about it. Is this the best number to reach you at if we call you on_____?
Thank you very much we are looking forward to seeing you on_____

APPENDIX 5: CONFIRMATION LETTER FOCUS GROUP.

Participants Name and Address
Dear
Thank you for agreeing to participate in the focus group that the University of Tasmania is holding on _____date at _____time at the Manukau Institute of Technology North Campus.
Enclosed with this letter is a map and directions which show you how to get to the Manukau Institute of Technology. There is free parking available on site. We will be meeting in room _____ and the staff at the front desk will be happy to show you where that room is.
As we explained in our earlier telephone call, the purpose of this group is to discuss your experiences of clinical drug trials. You will be part of a group of about six to eight people mainly from the local area who have had some involvement in clinical drug trials. We know that people have a great many different ideas on clinical drug trials, and we are very interested in hearing your thoughts on this subject.
The session will begin at _____ and end at _____. Refreshments will be provided at the start of the Focus group. We know how valuable your time is, and we will respect everyone's schedules by both starting and ending on time. So, please allow yourself enough time to reach the Manukau Institute of Technology by _____.
As we told you in our telephone conversation, we will be recording your discussion so we can keep a careful record of the things that we hear from you and the others. We will, as we promised, take every step to maintain your privacy. Expenses as a result of participation in the project will be reimbursed
Once again, we are glad you have accepted our invitation to participate in this group. Of course, the success of any group depends on each of its members, so we are counting on you. If you cannot attend for any reason can you please call me on 5345748 as soon as possible.
I look forward to meeting with you on _____
Sincerely yours,

Lyn Murphy
Investigator

APPENDIX 6: FOCUS GROUP CONSENT FORM.

Focus Group Consent Form

A cost benefit analysis of conducting sponsored clinical drug trials in a publicly funded New Zealand hospital.

REQUEST FOR INTERPRETER

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai

I have read and I understand the information sheet dated _____ for volunteers taking part in the study designed to identify the costs and benefits of conducting clinical drug trials. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my continuing health care.

I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I have had time to consider whether to take part.

I consent to the focus group interview being video-taped. YES/NO

I would like the researcher to discuss the outcomes of the study with me. YES/NO

I _____ (full name) hereby consent to take part in this study.

Date
Signature
Full names of Researchers
Contact Phone Number for researchers
Project explained by
Project role
Signature
Date

STATEMENT OF APPROVAL

This study has received ethical approval from the Northern Y Regional Ethics Committee Ethics Committee, ethics reference number NTY/09/04/037

This study has also been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au <mailto:human.ethics@utas.edu.au>. The Executive Officer is the person nominated to receive complaints from research participants. Please quote the ethics reference number H10522

Private Bag 86 Hobart
Tasmania 7001 Australia
Phone (03) 6226 2266 Fax (03) 6226 7845

School of Accounting & Corporate Governance

SURVEY INFORMATION SHEET

A cost benefit analysis of conducting sponsored clinical drug trials in a publicly funded New Zealand hospital.

INTRODUCTION:

You are invited to take part in a survey that we are conducting on the costs and benefits of clinical drug trials. Your participation in this study is entirely voluntary, and if you decide not to take part in the study, this will have no effect on your relationship with Counties Manukau District Health Board or your ongoing treatment.

This is a New Zealand based research project which is being supervised by the University of Tasmania.

CONTACTS

Investigator:

Lyn Murphy, PhD Student University of Tasmania, Manukau Institute of Technology, Bairds Rd, Otara, Manukau City Phone: 968 8000. Email lyn.murphy@manukau.ac.nz

Supervisor:

Dr William Maguire**,** Senior lecturer School of Accounting and Corporate Governance**,** University of Tasmania**,** Private Bag 86**,** Hobart**,** Tasmania 7001**,** Australia**.** Email: william.maguire@utas.edu.au

Co supervisor:

Dr Willem Fourie, Deputy Head of the Department of Nursing and Health Studies, Research Development Leader Manukau Institute of Technology Otara Rd Otara. Manukau City Phone: Work: 968 8606 Mobile: 027 5688606 Email willem.fourie@manukau.ac.nz

ABOUT THE STUDY

What are the aims of the study?

The purpose of this study is to find out about the costs and benefits of clinical drug trials.

How were participants selected for this study, and who selected them?

Participants were selected by the researchers from those recently involved in a clinical drug trial which took place at Middlemore Hospital.

What are the benefits of the study?

This study will assist us to better understand the costs and benefits of clinical drug trials.

What are the risks and/or inconveniences of the study?

We have not identified any risks in taking part in this study.

This is a non-therapeutic study

PARTICIPATION

Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part this will not affect any future care or treatment.

GENERAL

Where can I get more information about the study?

Contact the researchers whose names and details are provided on the first page of this information sheet. You do not have to answer all the questions, and you may stop the survey at any time.

CONFIDENTIALITY

No material which could personally identify you will be used in any reports on this study. We will keep your answers to the survey questions completely confidential. The surveys will be securely stored at Manukau Institute of Technology for 10 years after which time they will be destroyed.

RESULTS

The surveys form part of a large PhD project. If you wish the results of the survey can be sent to you shortly after the surveys have been completed.

STATEMENTS OF ETHICAL APPROVAL

This study has received ethical approval from the Northern Y Regional Ethics Committee, ethics reference number NTY/09/04/037

If you have any questions or concerns about your rights as a participant in this research study you can contact an independent health and disability advocate. This is a free service provided under the Health and Disability Commissioner Act.

Telephone: (NZ wide) 0800 555 050

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Email (NZ wide): advocacy@hdc.org.nz

This study has also been approved by the Tasmanian Social Science Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au <mailto:human.ethics@utas.edu.au>. The Executive Officer is the person nominated to receive complaints from research participants. Please quote the ethics reference number H10522

APPENDIX 8: FOCUS GROUP, INTERVIEW AND SURVEY QUESTIONS.

1. How does the international community benefit from clinical drug trials?

2. What are the risks, tradeoffs, disadvantages or costs to the international community in conducting clinical drug trials?

3. How do pharmaceutical companies benefit from clinical drug trials?

4. What are the risks, tradeoffs, disadvantages or costs to pharmaceutical companies in conducting clinical drug trials?

5. How do other New Zealanders benefit from clinical drug trials performed in Counties Manukau?

6. What are the tradeoffs, disadvantages or costs to other New Zealanders in Counties Manukau conducting clinical drug trials?

7. How does Counties Manukau District Health Board benefit from sponsoring clinical drug trials?

8. What are the tradeoffs, disadvantages or costs to Counties Manukau District Health Board in conducting clinical drug trials?

9. How do staff benefit from clinical drug trials performed at Middlemore Hospital?

10. How do staff benefit from clinical drug trials performed at Middlemore Hospital?

11. What are the tradeoffs, disadvantages or costs to Middlemore Hospital staff in conducting clinical drug trials?

12. How do participants benefit from being part of a clinical drug trial?

13. What are the tradeoffs, disadvantages or costs to participants in being involved in a clinical drug trial?

14. How do the care givers of trial participants benefit from clinical drug trials?

15. What are the tradeoffs, disadvantages or costs to the care givers of trial participants in being involved in a clinical drug trial?

APPENDIX 9: ECONOMIC OUTCOMES STRAND: TABLES OF RESULTS

TABLE A4.1: COST REVENUE STREAMS STUDY 1

	Trial Recruitment		Study Period				Follow-up Period		
	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/09	2009/10
Income	**40,306**	**204,649**	**129,547**	**69,689**	**92,058**	**191,962**	**74,646**	**9,245**	-
TOTAL REVENUE	**40,306**	**204,649**	**129,547**	**69,689**	**92,058**	**191,962**	**74,646**	**9,245**	-
Senior Medical Officer	-	-	500	5,538	7,602	21,107	12,833	1,325	-
Registrars	-	-	-	-	6,000	3,523	20,703	-	-
Total Medical Personnel	**-**	**-**	**500**	**5,538**	**13,602**	**24,630**	**33,536**	**1,325**	**-**
Registered Nurses	-	-	11,141	51,645	45,495	51,709	45,690	584	-
Nursing - Accident Compensation Commission (ACC) Levy	-	-	-	524	256	-	-	-	-
Nursing - Courses, Study Fees	-	-	-	-	-	-	516	-	-
Total Nursing	**-**	**-**	**11,141**	**52,169**	**45,751**	**51,709**	**46,206**	**584**	**-**
Technicians	-	-	-	-	-	-	1,338	-	-
Total Allied Health	**-**	**-**	**-**	**-**	**-**	**-**	**1,338**	**-**	**-**
Managers	-	-	-	-	-	-	748	-	-
Administration, Clerical							2,435	-	-

and Secretarial Staff	28,122	103,197	72,829	23	-	1,919			
Management and Administration - Courses, Conferences and Study	-	-	589	-	-	-	375	-	-
Total Management and Administration	**28,122**	**103,197**	**73,418**	**23**	**-**	**1,919**	**3,559**	**-**	**-**
Total Personnel	**28,122**	**103,197**	**85,059**	**57,730**	**59,352**	**78,258**	**84,639**	**1,909**	**-**
Outsourced Services									
Fee for Service Senior Medical Officer	-	-	-	3,925	-	-	-	-	-
Total Outsourced Personnel	**-**	**-**	**-**	**3,925**	**-**	**-**	**-**	**-**	**-**
Laboratory Service	-	-	-	4,299	852	3,073	1,797	-	-
Laboratory Sendaway Tests	-	4,655	6,504	1,698	775	1,900	-	-	-
Radiology Service	-	-	37,055	-	-	-	-	-	-
Outsourced Clinical Services Other	(7,352)	15,594	3,504	-	-	-	-	-	-
Provider Audit and Monitor	(1,332)	3,725	-	-	-	-	-	-	-
Total Outsourced Services	**(8,684)**	**23,974**	**47,063**	**5,997**	**1,627**	**4,974**	**1,797**	**-**	**-**
Total Outsourced	**(8,684)**	**23,974**	**47,063**	**9,922**	**1,627**	**4,974**	**1,797**	**-**	**-**
Syringe Needle and Sharps Bins	-	-	-	-	-	-	85	-	-
Patient Consumables	-	67	86	1,420	-	-	-	-	-
Electrodes	-	-	-	310	-	-	-	-	-
Recording Paper, Tapes and Disks	-	-	-	-	-	-	340	-	-

Testing Kits	-	-	-	-	420	2,194	1,494	-	-
Other Diagnostic Supplies	592	-	-	-	-	-	-	-	-
Batteries	-	-	-	-	-	-	12	-	-
Clinical Equipment Minor Purchases	673	-	686	600	956	-	-	-	-
Patient Welfare and Incentives	-	-	23	50	-	28	22	-	-
Patient Transport and Lodging	-	-	267	3,247	3,208	1,324	1,112	-	-
Total Clinical Supplies	**1,265**	**67**	**1,062**	**5,627**	**4,583**	**3,546**	**3,067**	**-**	**-**
Rents	-	-	-	-	35	-	-	-	-
External Storage Services	-	-	-	-	6	-	-	750	-
Fuel	-	-	1,000	889	2,955	5,222	2,300	-	-
Taxis	-	-	-	-	-	13	-	-	-
Staff Travel Domestic	-	-	-	-	9	-	26	-	-
Staff Travel International	-	-	-	-	-	-	13,976	-	-
Staff Accommodation and Meals	-	-	-	-	448	-	28	-	-
Information Technology Depreciation	-	-	-	279	368	368	582	597	498
Hardware Purchases <$500	-	-	-	-	-	-	(455)	-	-
Telecommunications Local and Toll Charges	-	533	628	711	809	78	89	609	450
Mobile Phones	-	-	389	528	1,144	687	902	94	-

Insurance	-	-	-	-	1,000	1,000	917	-	-
Other Equipment Purchases <$500	-	-	-	18	-	-	598	-	-
Printing and Forms	-	-	255	542	273	124	138	9	-
Stationery and Supplies	23	1,064	85	111	67	32	28	-	-
Postage Courier Freight	-	-	-	-	-	1,903	86	-	-
Other Office Expenses	889	8,330	4,801	271	56	192	53	-	-
Books Periodicals Journals	-	-	-	-	-	2,282	-	-	-
Advertising	320	1,072	-	-	-	-	-	-	-
Staff Support	-	840	-	-	-	-	-	-	-
Staff Relations	-	-	-	-	-	-	6	-	-
Sundry	-	(7)	12	-	-	-	-	-	-
Total Non Clinical	**1,232**	**11,833**	**7,172**	**3,348**	**7,170**	**11,900**	**19,273**	**2,059**	**947**
Net Surplus	**18,371**	**65,578**	**(10,809)**	**(6,938)**	**19,325**	**93,284**	**(34,129)**	**5,278**	**(947)**
PI Share									
CCRep Share									**149,014**

TABLE A4.2: COST REVENUE STREAMS STUDY 2

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/09	2009/10
Income	-	124,331	41,267	42,030	30,486	28,216	15,912	10,956	
TOTAL REVENUE	**-**	**124,331**	**41,267**	**42,030**	**30,486**	**28,216**	**15,912**	**10,956**	**-**
Registered Nurses	-	2,077	8,292	24,906	25,051	28,909	18,433	455	-
Nursing - Courses, Study Fees	-	-	628	(70)	-	-	-	-	-
Total Nursing	**-**	**2,077**	**8,919**	**24,836**	**25,051**	**28,909**	**18,433**	**455**	**-**
Administration, Clerical and Secretarial Staff	14,379	32,733	20,613	-	-	-	779	(59)	-
Management and Administration - Meals	-	-	-	-	50	-	-	-	-
Management and Administration - Courses, Conferences and Study	-	-	-	-	250	-	-	-	-
Total Management & Administration	**14,379**	**32,733**	**20,613**	**-**	**300**	**-**	**779**	**(59)**	**-**
Total Personnel	**14,379**	**34,810**	**29,532**	**24,836**	**25,350**	**28,909**	**19,212**	**396**	**-**
Outsourced Services									
Laboratory Service	-	-	-	1,278	445	-	318	-	-
Laboratory Sendaway Tests	-	3,763	4,082	407	268	113	2,882	-	-
Other Radiology Procedures	-	-	-	-	-	142	30	-	-
Outsourced Clinical Services Other	-	-	-	-	20	-	-	-	10,144
Total Outsourced Services	**-**						**3,230**	**-**	**10,144**

		3,763	**4,082**	**1,685**	**732**	**255**			
Total Outsourced	**-**	**3,763**	**4,082**	**1,685**	**732**	**255**	**3,230**	**-**	**10,144**
Containers and Bags	-	-	-	15	-	-	-	-	-
Continence and Hygiene Supplies	-	21	-	-	-	-	-	-	-
Dressings	-	-	-	-	-	17	-	-	-
Protective Clothing	-	20	-	-	-	-	-	-	-
Patient Consumables	-	23	81	-	-	-	-	-	-
Electrodes	-	-	-	-	-	140	-	-	-
Recording Paper, Tapes and Disks	-	-	-	48	92	63	(6)	-	-
Other Diagnostic Supplies	-	4,500	(8,487)	43	-	-	-	-	-
Batteries	-	-	-	13	-	-	-	-	-
Monitoring Equipment	-	-	-	15	-	-	-	-	-
Clinical Equipment Minor Purchases	229	2,886	-	781	19	-	-	-	-
Patient Welfare and Incentives	-	-	-	50	26	-	-	-	-
Patient Transport and Lodging	-	-	178	503	533	745	304	-	-
Total Clinical Supplies	**229**	**7,450**	**(8,229)**	**1,469**	**670**	**965**	**298**	**-**	**-**
Laundry Bedding and Linen	-	252	57	204	75	249	259	8	-
Rents	-	-	-	-	-	35	-	-	-
External Storage	-					-	-		-

Services		-	-	-	-			750	
Fuel	-	-	-	-	-	187	110	-	-
Taxis	-	-	-	-	-	4	41	-	-
Staff Travel Domestic	-	-	237	844	13	91	49	-	-
Telecommunications	60	-	-	-	-	-	-	-	-
Telecommunications Line Rentals	60	56	-	-	-	-	-	-	-
Telecommunications Local and Toll Charges	-	75	7	10	7	26	45	3	-
Affiliation Fees	-	350	-	-	-	-	-	-	-
Insurance	-	-	-	-	1,000	1,000	751	-	-
Other Equipment Purchases <$500	-	-	-	18	-	172	-	-	-
Printing and Forms	44	150	188	324	172	162	87	-	-
Stationery and Supplies	216	3,495	94	144	105	21	20	-	-
Postage Courier Freight	4	5	10	28	27	164	-	-	-
Other Office Expenses	129	117	622	53	79	6	6	-	-
Staff Support	-	144	-	-	-	-	-	-	-
Sundry	-	400	-	-	-	-	-	-	-
General Expense	-	500	-	-	-	-	-	-	-
Total Non Clinical	**513**	**5,543**	**1,214**	**1,624**	**1,476**	**2,118**	**1,369**	**761**	**-**
Net Surplus									**(10,144)**

	(15,121)	72,765	14,667	12,416	2,257	(4,031)	(8,196)	9,799	
PI Share									30,432
CCRep Share 15%									43,980

TABLE A4.3: BENEFIT COST ANALYSIS CCREP

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/09	2009/10
TOTAL REVENUE	40,306	328,980	170,814	111,719	122,544	220,177	90,559	20,201	
Personnel	**42,501**	**138,007**	**114,591**	**82,566**	**84,703**	**107,167**	**103,850**	**2,305**	
Outsourced	**-8,684**	**27,737**	**51,145**	**11,607**	**2,358**	**5,229**	**5,027**		**10,144**
Clinical Supplies	**1,494**	**7,517**	**-7,167**	**7,096**	**5,254**	**4,510**	**3,364**		
Non Clinical	**1,745**	**17,375**	**8,386**	**4,972**	**8,647**	**14,018**	**20,642**	**2,820**	**947**
TOTAL COSTS	**37,056**	**190,636**	**166,955**	**106,241**	**100,961**	**130,924**	**132,883**	**5,125**	**11,091**
Net Cost Revenue	**3,250**	**138,344**	**3,858**	**5,478**	**21,583**	**89,253**	**(42,325)**	**15,076**	**(11,091)**
NPV @ 3.5%	**201,363**								
NPV @ 5%	192,905								
NPV @ 10%	168,321								
NPV at 3.5% per trial participant	799								

TABLE A 4.4: COST AVOIDANCE FROM PHARMACEUTICALS

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/9
Control	29,283	129,598	206,167	392,798	437,865	447,032	429,715	406,716
Control/2	14,642	64,799	103,084	196,399	218,932	223,516	214,857	203,358
Case	14,639	67,111	92,140	172,324	227,349	256,204	263,504	243,880
Total Control - Case	**2**	**(2,312)**	**10,943**	**24,075**	**(8,417)**	**(32,688)**	**(24,324)**	**(40,522)**
Per patient pharmaceutical costs: Control								
Control number	504	504	495	474	461	450	445	436
Control mortality		3	9	21	13	11	5	9
Total survival	504	495	474	461	450	445	436	436
Total pharmaceutical costs	29,283	129,598	206,167	392,798	437,865	447,032	429,715	406,716
Per patient pharmaceutical cost: Control	**58**	**262**	**435**	**852**	**973**	**1,005**	**986**	**933**
Per patient pharmaceutical costs: Case								
Case sample	252	252	250	247	247	243	238	234
Case mortality		2	3	0	4	5	4	1
Total survival	252	250	247	247	243	238	234	233
Total pharmaceutical cost	14,639	67,111	92,140	172,324	227,349	256,204	263,504	243,880
Per patient pharmaceutical cost: Case	**58**	**268**	**373**	**698**	**936**	**1,076**	**1,126**	**1,047**
Total pharmaceutical cost avoidance								
Control cost per patient	58	262	435	852	973	1,005	986	933
Case cost per patient							1,126	

	58	268	373	698	936	1,076		1,047
Control - Case	0	(7)	62	154	37	(72)	(141)	(114)
Per person savings x total surviving case	-	**(1,657)**	**15,293**	**38,134**	**9,098**	**(17,117)**	**(32,878)**	**(26,529)**
NPV @ 3.5%	**-3,681**							
NPV @ 5%	**-880**							
NPV @ 10%	**5,645**							

TABLE A 4.5: COST AVOIDANCE FROM LABORATORY TESTING

Cost avoidance: Laboratory Testing	**2001/02**	**2002/03**	**2003/04**	**2004/05**	**2005/06**	**2006/07**	**2007/08**	**2008/9**
Laboratory Testing Costs: Control Group	82,609	99,600	106,310	109,176	103,071	101,277	8,593	8,739
Laboratory Testing Costs Control Group / 2	41,304	49,800	53,155	54,588	51,535	50,638	4,297	4,369
Less Laboratory Testing Cost: Case	39,779	42,198	49,680	54,395	56,790	54,831	4,087	3,015
Total Cost avoidance	**1,525**	**7,602**	**3,475**	**193**	**(5,255)**	**(4,192)**	**210**	1,354
Average per Patient Laboratory Costs: Control								
Sample	504	504	495	474	461	450	445	436
Mortality		3	9	21	13	11	5	9
Total Survival	504	495	474	461	450	445	436	436
Laboratory Costs	82,609	99,600	106,310	109,176	103,071	101,277	4,297	8,739
Average Cost Per Patient	164	201	224	237	229	228	10	20
Average per Participant Laboratory Costs: Case								
Sample	252	252	250	247	247	243		238 234
Mortality		2	3	0	4	5		4 1
Total Survival	252	250	247	247	243	238	234	233
Laboratory Cost	39,779	42,198	49,680	54,395	56,790	54,831	2,043	3,015
Average Cost per Patient	158	169	201	220	234	230	9	13
Total Savings from Laboratory Testing								
Control Cost per Patient	163.91	201.21	224	237	229	228	10	20
Case Cost per Participant	157.85	168.79	201	220	234	230	9	13
Control - Case	6	32	23	17	(5)	(3)	1	7
Total Savings (Per person savings x total surviving case)	**1,525**	**8,105**	**5,718**	**4,101**	**(1,132)**	**(664)**	**263**	**1,655**

TABLE A4. 6: CHRONIC CARE MANAGEMENT (CCM) COSTS

CCM	**2001/02**	**2002/03**	**2003/04**	**2004/05**	**2005/06**	**2006/07**	**2007/08**	**2008/9**
CCM Enrolment	14	16	26	24	38	63	40	15
CCM Disenrolment	0	0	0	8	7	6	8	32
Enrolments minus Disenrolment	14	16	26	16	31	57	32	(17)
Enrolments minus Disenrolment / 2	7	8	13	8	15.5	28.5	16	(8.5)
Total Enrolments minus Disenrolment/2	7	15	28	36	51.5	80	96	87.5
Percentage CCM enrolments: control	2.78%	6.06%	11.81%	15.62%	22.89%	35.96%	44.04%	40.14%
Case: Chronic Care Management (CCM) costs								
CCM Enrolment	3	3	9	12	22	41	16	9
CCM Disenrolment	0	0	0	2	0	5	7	11
Enrolments minus Disenrolment	3	3	9	10	22	36	9	(2)
Total Enrolments minus Disenrolment	3	6	15	25	47	83	92	90
Percentage CCM enrolment case	1.19%	2.40%	6.07%	10.12%	19.34%	34.87%	39.32%	38.63%
Total Cost avoidance								
Control minus Case	4	9	13	11	4.5	(3)	4	(2.5)
Total Cost avoidance CCM @ $197.95	**792**	**0**	**2,573**	**2,177**	**891**	**(594)**	**792**	**(495)**
NPV @3.5%	5,497							

TABLE A4.7: COMBINED COST AVOIDANCE

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/9
Pharmaceutical Costs	-	(1,657)	15,293	38,134	9,098	(17,117)	(32,878)	(26,529)
Laboratory Testing	1,525	8,170	5,787	4,101	(1,151)	(678)	267	1,662
CCM	792	1,188	2,573	2,177	891	(594)	792	(495)
Total	**2,317**	**7,700**	**23,653**	**44,412**	**8,838**	**(18,389)**	**(31,819)**	**(25,362)**
NPV@3.5%	**$17,676**							

TABLE A4.8: DEPRECIATION INFRASTRUCTURE AND OVERHEAD COSTS

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/9
Clinical trials performed at CCRep	6	13	12	21	31	42	69	70
Allocation of indirect costs as a proportion of overheads	**19,507**	**22,324**	**25,149**	**27,984**	**30,826**	**33,678**	**36,539**	39,409
Trials 1 and 2 as percentage of total trials	33.33%	15.38%	16.67%	9.52%	6.45%	4.76%	2.90%	2.86%
Allocation of indirect costs to trials 1 and 2	**6,502**	**3,434**	**4,192**	**2,665**	**1,989**	**1,604**	**1,059**	**1,126**

TABLE A4.9: BENEFIT COST ANALYSIS CMDHB PERSPECTIVE

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08	2008/9
Net cost revenue from CCRep	**3,250**	**138,344**	**3,858**	**5,478**	**21,583**	**89,253**	**-42,325**	**15,076**
Cost avoidance	**2,317**	**7,687**	**23,839**	**44,412**	**8,988**	**-18,749**	**-15,661**	**-25,476**
TOTAL BENEFITS	5,567	146,030	27,697	49,890	30,570	70,504	-57,986	-10,400
Depreciation Infrastructure and Overheads	6,502	3,434	4,192	2,665	1,989	1,604	1,059	1,126
TOTAL COSTS	**6,502**	**3,434**	**4,192**	**2,665**	**1,989**	**1,604**	**1,059**	**1,126**
TOTAL BENEFIT MINUS COSTS	**(4,185)**	**4,252**	**19,648**	**41,747**	**6,999**	**(20,352)**	**(16,720)**	**(26,602)**
NPV @ 3.5%			$10,019.57					
NPV @ 5%			$11,597.43					
NPV @ 10%			$14,852.20					

TABLE A4.10:BENEFIT COST ANALYSIS FROM THE PERSPECTIVE OF NEW ZEALAND SOCIETY

	2001/02	2002/03	2003/04	2004/05	2005/06	2006/07	2007/08
Control mortality	3	9	21	13	11	5	9
Control mortality/2	1.5	4.5	10.5	6.5	5.5	2.5	4.5
Case mortality	2	3	0	4	5	4	1
Statistical life years (SLY) saved	(0.5)	1.5	10.5	2.5	0.5	(1.5)	3.5
Cumulative total SLY saved	(0.5)	1	11.5	14	14.5	13	16.5
SLY saved x Tariff 0.92	(0.46)	0.92	10.58	12.88	13.34	11.96	15.18
Discounted VSLY (Using base year 2008 and average 3% inflation)	281,563	289,972	298,633	307,552	316,737	326,197	335,939
VSLYx Tarriff x SLY	(129,519)	266,775	3,159,534	3,961,266	4,225,272	3,901,313	5,099,554
NPV @ 3.5%		$17,165,121					
NPV @ 5%		$15,952,878					
NPV @ 10%		$12,624,762					

END